1992

UWOMJ Volume 62, Number 1, Fall 1992

Western University

The UNIVERSITY *of* WESTERN ONTARIO

MEDICAL JOURNAL

- An interdisciplinary medical science publication; established 1930 -

Volume 62 Number 1 Fall 1992

INSIDE THIS ISSUE:

- Chemical Dependency & Mental Illness
- Cocaine Toxicity
- Designer Drugs
- Toad Licking
- Drug Research Update
- Report from Betty Ford Center

On call 24 hours a day

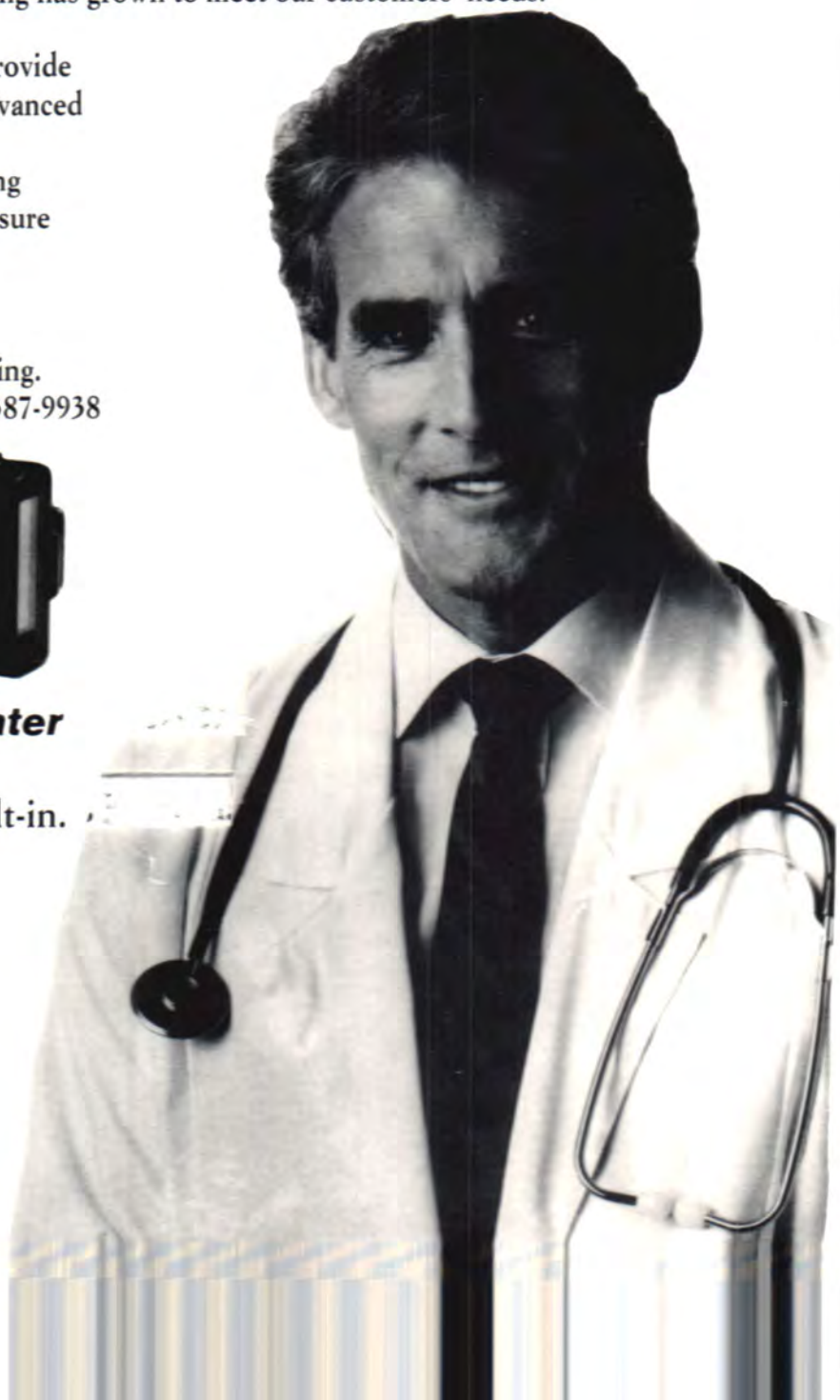
Trust Maclean Hunter for exceptional paging products and services, and you'll be accessible any place... all the time. With almost 20 years of experience, Maclean Hunter Paging has grown to meet our customers' needs.

We're equipped to provide you with the most advanced paging system and dependable answering services, so you'll be sure to get the message.

Make the move to Maclean Hunter Paging. Call us today: 1-800-387-9938

Maclean Hunter Paging

Our Reliability is Built-in.



Editorial Staff

On the Cover:

Counter-clockwise from the top:

1) *Amanita Muscaria* ("Fly agaric"). These mushrooms contain muscimol (a potent hallucinogen), ibotenic acid (a potent insecticide), and muscarine (a cholinergic agent). Used for over 3,000 years by Asian and Indian tribes. Findings are primarily anticholinergic because of insecticide content;

2) *Tabernanthe Iboga* (Ibogaine from Central Africa). Derived from the root; used for its anti-depressant and euphoric properties. Sometimes used as a substitute for cocaine.

3) *Papaver Somniferum* (Opium poppy of SW Asia). Cultivated as a source of opium;

4) *Cannabis Sativa* (Indian hemp plant). Dried pistillate used to make hashish; dried leaves and flowers used to make marijuana;

5) *Crocus Sativa* (Meadow saffron). A colchicine-containing plant that causes mitotic poisoning. Toxicity can occur after a partially dose-dependent latent period associated with ingestion of seeds, bulbs, and flowers. Saffron has been used successfully for suicide;

6) Sundry items of substance abuse (pills, syringes, and "joints").

Cover art by Joe Kim, Meds '96

UPCOMING SUBMISSION DEADLINES:

Winter 1993 Issue (Feature Section: Gerontology)
- Journal articles ..... January 10, 1993
- Communiques, book reviews, & art work: ..... January 17, 1993

Spring 1993 Issue (Feature Section: Ophthalmology)
- Journal Articles: ..... March 26, 1993
- Communiques, book reviews, & art work: ..... April 09, 1993

CONTENTS

Chemical Dependency
(P. 17)

MPTP & MDMA
(p. 24)

Research Update
(P. 35)

The U.W.O. Medical Journal is an interdisciplinary medical science publication, established in 1930. The Journal is published three times each academic year: Fall, Winter, & 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.

APPROACHES TO SUBSTANCE ABUSE

Drugs of abuse consist of those which are entrenched in our way of life (like alcohol and tobacco) and those which are illegal (like cocaine, heroin, cannabis, amphetamine, etc.). Current problems associated with drugs of abuse include failure to eradicate substance abuse, excessive morbidity and mortality consequent to substance abuse, and the financial burden of drug-related health problems to the health care system (see inset).

In order to gain some idea of the current approach to problems associated with substance abuse, I spoke with Alan Ogborne, a senior scientist (programs and services evaluation, research department) at the Addiction Research Foundation (ARF) in London. Clearly, there are no hard fast solutions to the problems of substance abuse. The ARF recently outlined some objectives to be accomplished by the year 2000[1]. These objectives included reductions in alcohol use by 25%; cocaine and crack use by 50%; and alcohol-related traffic fatalities to 15% (from 50%). As well the ARF is aiming for a balanced, appropriate, and accessible treatmentservice system. Current programs designed to achieve these goals are aimed at reducing the demand for drugs, as opposed to the supply--supply reduction has proved very costly and very ineffective.

Programs designed to reduce demand include those emphasizing health promotion and education (i.e. creating an awareness of the effects of drugs) and programs designed to treat people who require assistance and therapeutic intervention. According to Hans Embald, director of the World Health Organization (WHO) on substance abuse, strategies to reduce drug abuse should be based on recognition of political and economic realities of people's lives[2]. In the past, addictive drugs have been viewed as having mystical powers to not only induce "positive" psychologic and physiologic effects, but to siphon an individuals' ability to make a choice as well. The WHO recommends that programs to reduce drug abuse shouldn't focus only on the harmful and mystical properties of drugs thereby glamourizing them, but should challenge the drugs' "positive" effects and remove the glamour associated with them. These steps will allow education to progress. Programs developed within Ontario to discourage substance abuse include *Drug Awareness Week, Server Intervention, R.I.D.E., Sober Driver, Just Say No,* and *Alcohol on Campus.*

Treatment facilities and programs exist which are more suitable to reduce demand in people who have developed dependencies or are likely to. The ARF has developed an early intervention program designed to help people who have drinking problems but are not yet dependent on alcohol. This approach has gained support because of a potentially high success rate, the low costs, and the prospect for preventing more serious problems. Programs also exist to help people with drug dependency. Programs in Ontario include *Detoxification,* which provide a safe, supervised setting for drug withdrawal; *Assessment/Referral,* which assess people with alcohol and other drug problems; *Non-Residential,* which provide treatment, rehabilitation, and/or aftercare; *Short-term Residential,* which offer structure, intensive treatment and/or rehabilitation for 40 or fewer days; and *Long-term Residential,* such as recovery homes and halfway houses. Treatment programs for tobacco addiction are usually offered by other organizations such as the *Lung Association,* the *Canadian Cancer Society,* and other commercial organizations. A number of programs now incorporate, alcohol, tobacco, and other drugs.

***Some facts*[1,4]:**

** 1985 Ontario deaths related to drug use: 20,006 (30% of total); 13,375 deaths associated with tobacco, 6,506 related to alcohol, and 125 related to illegal drugs.*

** Leading cause of death < 35: accidents and violence (50% related to drinking); leading causes of death 35-64 include lung cancer and chronic liver disease (heavily linked to alcohol and tobacco).*

** Number of alcohol-related offenses in Ontario in 1990: 106,851; number of offenses related to illicit drugs was 25,532.*

** Cannabis is the most frequently used illicit drug; cocaine is used much less frequently; crack use is rare.*

** The number of alcohol and drug treatment programs in Ontario in 1988-89 was 217; most common drug problem in the treatment system: alcohol; percent change in the number of people treated in the addictions treatment system from 1979-89: +102%.*

** 1991-92 gov't revenue from tobacco tax: $1,028 M (2.5% of total); revenue from LCBO profits and liquor-related sales: $1,158 M (2.8% of total).*

** Total health care costs to Ontario related to drug abuse is estimated at $5.5 B.*

** Indicators of alcohol and drug problems in Ontario suggest a recent decline.*

Mutual aid groups, such as *Alcoholics Anonymous*, the *Betty Ford Center*, *Narcotics Anonymous*, and *Women for Sobriety* also aim at helping people recover from addiction through social support. Finally, other people and facilities offering drug treatment include general and psychiatric hospitals, mental health clinics, counselling agencies, and probation and correctional services.

Controversy undoubtedly exists as to the effectiveness of various programs. An article by Holder et al. analyzed different treatment facilities for alcoholism based on effectiveness, benefits, and costs.[3] Their results suggested that residential/milieu treatment programs (e.g. Betty Ford, AA) were by far the least worthwhile, whereas brief motivational counselling, self-control training, and social skills training were among the best treatment modalities. Apparently many reports regarding programs like Betty Ford tend to be based on testimonial evidence from "program graduates" and uncontrolled studies using "graduates" as subjects. As well enrolment in these programs is selective--applicants are chosen based on a willingness to seek aid and self-discipline. Many drug users don't have these characteristics.

Certainly, problems associated with drug abuse and addiction are the focus of much effort and attention. Ultimately, the ideal aim of treatment facilities is complete abstinence. For many people reduction in use to a non-hazardous level is a more realistic goal. The battle against substance abuse is uphill, but current efforts suggest forward progress.

Before closing, I would like to congratulate Ross and Shobhana, and the entire Journal Staff for a job well done. We've designed a new cover utilizing school colours and the new faculty crest. We've also incorporated a new section called Faculty News to promote the Journal as a communication medium for the Faculty of Medicine and the London Medical Community. A coordinated effort and informative articles have helped produce a very good issue! I would also like to welcome Dr. McMurtry as the new Dean of the Faculty of Medicine. On behalf of the Journal I wish him good fortune, and I hope that the school profits from his wisdom.

Ω

Jeffrey Politsky,
Editor.

1) ARF Report. Drugs In Ontario. 48 pp (1990).
2) ARF Journal 21(5):1992.
3) Holder H., et al. J. Stud. Alcohol.52:517-40 (1991).
4) Ministry of Treasury and Economics. 1992 Ontario Budget. 115 pp. (1992).

DEANS' CORNER

This marks the first effort toward what we hope will become a regular feature in the journal. You will note from the position of the apostrophe in the title that the column is not just for the Dean himself to communicate with you, but also will reflect issues, plans, projects, trial balloons, and the flotsam and jetsam that any of us in the Dean's office might feel would be of interest to the readership. For those readers who have been away from Western for a while, you may be interested to know that the Dean's office is currently configured into six divisions. As a result, there are Assistant Deans for curriculum (David Hollomby), education (Bob Barr), clinical affairs (Jim Silcox), postgraduate education (Bessie Borwein), and continuing education (Keith Paton). Besides this, we have the Office of Health Sciences Education, better known by its acronym, "OHSED", directed by David Lloyd. We hope that future issues will provide a forum for each of them to speak to you.

In this first column, it seemed timely to talk a bit about career selection. In high school, we used to refer to this as guidance, and, there is long tradition at that level of trying to help students to make informed academic decisions leading them to the career of their choice. Medical schools never went in much for that sort of thing, even though the decisions that medical graduates have had to make have been every bit as bewildering as those that faced them when they left high school. Students were left to lurch into their lifelong medical careers by good luck, intuition, or fate...perhaps all three. Sometimes it worked; sometimes it didn't.

Now that the rules for licensure have changed and internship is a thing of the past, the first post graduate year is already a streaming year which sets the student on the path to her or his ultimate practice pattern. This has meant that these men and women must be well informed about the vast array of career options open to them. This is no mean trick to achieve by the summer and fall of fourth year when they make their applications to post graduate programs and prioritize their submissions to C.I.M.S. Needless to say, this has generated a lot of anxiety amongst students. It seems as if they have barely been admitted to medicine before they must start searching around for the answers that they need in order to select the post graduate training that is right for them. As if undergraduate medicine wasn't stress enough already!

At Western, we have developed two new initiatives to help. The first is the Glaxo Pathway Evaluation Program. Sponsored by Glaxo Canada, this program is composed of three parts. In November of third year, during a week long orientation to phase IV, workshops will be held in which we teach the class a methodology for making decisions and give the students a chance to practice it. At the workshop, we provide the important second component of the program. Each student will get a binder, really a compendium, which contains relevant information about every specialty practised in Canada, including Family Medicine. This book contains details of training programs plus a lot of practical information about income, lifestyle, practice pros and cons, etc. The final part of the program is to encourage students to use the forthcoming clerkship not only to learn about clinical medicine but also as a window on the various career options that they can take. As they start a block, they should identify the career questions that they want answered by the time they leave the service. They are encouraged to ask residents and consultants to talk about their perceptions about their career choice. In other words, the clerkship should be viewed as a career-guidance experience as well as a content/skill/attitude learning experience.

To complement this program, we will be launching in the new year a career fair or career night program. (We haven't quite settled on the format yet.) This will be targeted more at first and second year classes and will give an opportunity for representatives of the various specialities to meet the students, provide them with information about their own specialities and answer questions. Although some have referred to this as "recruiting", we are aiming for informality and a way to plant seeds in the minds of students who want information early in order to think a bit and perhaps focus their later inquiries.

The result of all of this is that many physicians outside and inside the faculty will be subjected to a lot more questions from students about why they chose their areas of practice. I encourage all to take the time to respond honestly and thoughtfully. Now more than ever, our colleagues of the future are depending on us.

Ω

Jim Silcox, M.D.,
Assistant Dean,
Student Affairs & Undergraduate Studies.

HIPPOCRATIC COUNCIL NOTES

The 1992-93 Hippocratic Council, in association with the Meds Journal will be providing this column to improve communication between the Council, the student body, and the Faculty of Medicine. It is our hope that this column will generate interest and new ideas for students both within the faculty at Western and at other Canadian Medical Schools.

A special welcome to the Class of Meds ' 96, and a pat on the back to Meds '95 for a job well done during orientation. The Fanshawe Park Picnic was once again a great way to forget the summer! The recent Health Sciences Pub was a huge success - thanks to Liisa Honey (Social VP) and all who volunteered their time.

So, what exactly does the Hippocratic Council do? A lot! For one, we keep Medical students in touch with issues by representation and participation on councils at Western (eg. UMEC, Student Affairs, USC) and throughout the country (eg. CFMS, the Canadian Federation of Medical Students). Last May, Katherine Wise (past VP-Executive), Stephanie Windsor (past Community Relations Rep.) and Merrilee Brown (Secretary) attended a conference on the evaluation of medical students held by the EFPO (Educating the Future Physicians of Ontario). Recently, Lesley Horton and Ambrose Au (External Liaison Officers) traveled to Vancouver to attend the National Conference of the Canadian Federation of Medical Students. The subject of post-graduate licensure and recent changes in the MCCQE examination formats were discussed. On October 16, Stephen Burnett (VP-Executive) attended a conference at Dalhousie on Confidential Counseling and Support Systems in Medical Schools. Both student and administrative representatives from medical schools in Canada, the U. S., and Great Britain attended. The issues of confidentiality and availability of services to students were discussed as important factors in an effective support system. The Council is also involved in the community through donations to various organizations and charities, including Med Outreach and the London Food Bank.

The first in a series of "Brown Bag" lunches was held on October second. Dr. R. M. Barr, Assistant Dean of Postgraduate Medical Education spoke on the recent changes in post-graduate licensure and the implications of making earlier career choices. As always, many questions were generated and problems discussed. The Student Affairs and Learning Skills Committee presents these sessions in an effort to address the concerns, interests, and questions of students on issues which will affect them now and in the future. Watch for posters displaying upcoming speakers, including ethics seminars!

By the time you read this, the Car Rally, Homecoming, and Oktoberfest will all have taken place. Future events sponsored by the Hippocratic Council include Tachycardia (Feb. 9-13) , a Food Drive , and the Meds Formal (early April - ALL YEARS AND CONSULTANTS INVITED!). Also be sure to watch for the health sciences variety night, "Tachycardia"- coming soon!

Janice Barkey (Meds ' 95) has been appointed by the Council to sit on the Medical Sciences Renovation and Planning Committee to keep students updated on construction (to begin in Feb. 1993) in the Medical Sciences Building. The changes planned will involve the Medical Students Lounge, Hippocratic Council and Meds Journal offices, CBLC (Computer Based Learning Center), and Learning Resources Centre.

The members of the Hippocratic Council are your student representatives, and greatly value your suggestions and comments regarding Medicine at Western. If you would like to discuss any issues or events, or have any ideas, we encourage you to contact any member of the council :

Mark Mensour,	(President, '94)
Ambrose Au,	(VP Academic, '95)
Stephen Burnett,	(VP Executive, '94)
Liisa Honey,	(Social, '94)
Ingrid Tiessen,	(Treasurer, '94)
Merilee Brown,	(Secretary, '95)
Elyse Lackie,	(Past President, '93)
Leslie Horton,	(Ext. Liason Officer, '94)
Ambose Au,	(Ext. Liason Officer, '95)
Mohammed Moussa,	(USC Rep., '95)
Natalie Nimetz,	(Comm. Relations Dir., '95)
Jon Riddel,	(Athletic Rep., '94)
Katie Klein,	(Athletic Rep., '94)
Jeff Politsky,	(Meds Journal Ed., '94)
Ross Mantle,	(Meds Associate Ed., '95)
Shobhana Patel,	(Meds Associate Ed., '94)
Greg Hancock,	(Tachycardia Rep., '93)
David Fisman,	(Tachycardia Rep., '94)
Debbie Peneva,	(Meds '94 Class President)
Britt Carlson,	(Meds '95 Class President)
Jason Hodge,	(Meds '96 Class President)
Janice Barkey,	(Renovation Rep.)
Dr. John Howard,	(Honourary President)

Ω

Mark Mensour and Stephen Burnett

CBLC & LRC UPDATE

Renovations

Unexpectedly, this past summer the Province announced it would provide $2.6 million in funding through "Jobs Ontario Capital" for renovations to the M139 area of the Medical Sciences Building. The renovated area will provide: three additional classrooms, eight small group teaching rooms, a larger Learning Resource Centre (LRC) and Computer Based Learning Centre (CBLC), office space for the Meds Journal and the Hippocratic Council, and a new medical student lounge and study room. The office of Instructional Resources will also relocate to the renovated area. The final design has not been completed but the anticipated start date for reconstruction of the area is January of 1993. Students will be notified of the exact date the area will be closed off and the locations of the temporary sites for the Student Lounge, Computer Based Learning Centre, and Learning Resource Centre. Janice Barkey (Meds' 95) is the student representative and liaison on the planning committee and the Hippocratic Council. Student input into the design of the area is welcomed.

Nursing Student Access

Another new change in the CBLC/LRC has been the addition of access to Nursing students. The Faculties of Nursing and Medicine are collaborating in the expansion of the LRC/CBLC and pooling their learning resources for mutual student use. A new staff person has been added by the Faculty of Nursing to assist in the Centre. Kathryn Morton joined the Learning Resource Centre in October of this year and is available to provide students and faculty with assistance in the Learning Resource Centre.

Summer Student Projects

Two instructional resources completed this summer by Leila Kasrai, Janice Barkey and Margherita Cadeddu are available for use in the LRC:
(i) The Rectal Exam Module provides complete instruction on performing a rectal exam. Within the module the slide/tape program describes the procedure step by step and with the poster displays, shows examples of some of the more common lesions one may encounter during inspection. A male anatomical model of the pelvis and pathology specimens are also available. Finally, a prostate exam mannequin and manual provides an immediate opportunity for practising your skills.
(ii) The Pelvic Exam Module is composed of a detailed instructional videotape demonstrating a female pelvic exam, a female anatomical model of the pelvis, pathological specimens, and pelvic exam mannequins with a manual for practice.

New Programs/Materials

The following materials have recently been added to the collection:

Computer Assisted Instruction:
"AIDS: Vignettes for Physicians";
"Cardiovascular Physiology: Lab Experiments" (Macintosh/Videodisc);
"Epidemic in a Small Town: Introduction to the Epidemiologic Process" (Macintosh/Videodisc);
"Human Reproduction and Development";
"HyperHistology" (Macintosh/Videodisc);
"The Impotent Patient" (Infowindow/Videodisc);
"Right to Die? The Case of Dax Cowart" (Infowindow/Videodisc);
Videotapes:
"A.I.D.S.: Fears and Feelings";
"Breaking Bad News";
"The Gynecological Teaching Assistant: Pelvic and Breast Exam";
Mannequins:
Breast Exam Simulators;
Pelvic Exam Simulators with manual;;
Prostate Exam Simulator with manual
Slide/Tape Programs:
"Clinical Methods: The Rectal Exam";
Reference Texts:
"The Art and Science of Bedside Diagnosis";
"Atlas of Chest Infections";
"Atlas of Gastrointestinal and Hepatobiliary Infections";
"Atlas of Infections of the Skin";
"Atlas of Sexually Transmitted Diseases";
"The Ciba Collection of Medical Illustrations" Vols. 1-8;
"Color Atlas of Allergy Series";
"A Guide to Physical Examination and History Taking";
"Infectious Diseases Text and Color Atlas";
"Microbiology Scope Publication Series";
"Principles and Practice of Infectious Diseases";

CD-ROM

Scientific American Medicine "Consult". This is a subscription to a continuously updated compendium of medical information which is indexed and searchable. The resource includes both graphics and text. We are very pleased to be able to offer CD-ROM for the first time in the CBLC.

Reference texts, slide/tape programs, and computer assisted instruction on the DOS based system of terminals are accessible to Medical and Nursing

students around the clock in the LRC. Videotapes and mannequins are currently only accessible when the CBLC is open.

In Progress

We are pursuing funding from the GradPact* and Foundation Western for a number of new materials as well as Medline in the CBLC. We feel that a Medline service would be an appropriate addition to the centre in the near future. [Editor's note: Third party funding is also being sought independently by Hippocratic Council, preferrably for a multidisk server, licensed for network access in the CBLC. The contact person on Council is Ambrose Au. According to Ambrose, Western Medicine is one of only two medical faculties in Canada without free Medline access for students.] Access to electronic mail for students, a standard service for medical schools around the world who are connected via the interuniversity Vax network, is also on the drawing board. With this service, students could send and receive mail to universities around the world at low cost, with personalized billing through a system of access codes. The service also provides a large number of specialized bulletin boards for exchanging information.

Ω

Beth Thorstenson, CBLC/LRC Director

*The GradPact is a vehicle administered by Foundation Western through which students about to graduate may pledge money for the next three years to be used as the graduating class sees fit.

READ ANY GOOD BOOKS LATELY?

The Journal accepts Book Reviews. Please see page 3 for Submission Deadlines & page 51 for Guidelines to Authors.

TRIBUTE TO DEAN VALBERG

In June of this year, Dr. Leslie Valberg stepped down as Dean of the Faculty of Medicine at The University of Western Ontario after a seven-year term.

Leslie Valberg was born in 1930 in Churchbridge, Saskatchewan. He entered the six-year medical program at Queen's University in Kingston at eighteen and graduated with a Gold Medal in 1954. He completed residency training and a Master's Degree in biochemistry by 1958. After a year in England as a Medical Research Council Fellow, he took a position at Queen's for 15 years as Lecturer. His research included studies on absorption and metabolism of iron, zinc, and other heavy metals. He has become an authority on hereditary hemochromatosis. He served as Chief of Gastroenterology and Director of the Clinical

☞ 12

Investigation Unit at Kingston General Hospital, and received Queens' Aesculapian Society (medical school student council) Lectureship Award for excellence in teaching in 1966.

Dr. Valberg was Chairman of the Department of Medicine at The University of Western Ontario from 1975-85. In 1985, he was selected to be Western's new Dean of Medicine, a very high honour bestowed upon a physician.

When Dr. Valberg entered the position, Western's undergraduate medical curriculum was organized roughly along the lines recommended by Abraham Flexner some seventy-five years before: two "in class" years followed by two "in hospital" years. Today, the "in class" segment has been extended by almost five months due to the introduction of Problem-Based Learning.

Dr. Valberg has served the academic medical community in an eminent fashion for over thirty years, seven of those as our Dean. Through these efforts, his successor, Dr. McMurtry, has a strong legacy upon which to build his own vision of our medical school. We thank Dr. Valberg for leading us through the last seven years.

Ω

Meds '93

by Les Wright

Greetings all! Since fourth-year electives have tossed our class across the city, country, continent, and planet, there is little local Meds '93 news to report this time around. By the time this little missive is published, our mates will have returned from no doubt stimulating experiences in such places as England, Hawaii, Los Angeles, New York, Massachussetts, northern Quebec, Toronto, Kingston, and London, Ontario. Hopefully, all will make it home safely for class on November 30.

Of course, the spectre of internship and its concomitant application process dogs senior-year medical students no matter how much they try to hide. For those of you who have had early interviews, I hope they went well. For those of you awaiting responses, I wish you all the best. Incidentally, for anyone who still has not sorted it out, postgraduate education in Ontario as of June 1993 can be described as follows: there is no such thing as a "two-year internship"—there never was. One must pursue residency training of at least two years duration leading to certification either by the Canadian College of Family Physicians (in the case of Family Medicine training) or the Royal College of Physicians and Surgeons of Canada (in the case of specialty training) prior to being eligible for licensure. To this end, most Canadian faculties of medicine are offering Post-graduate-Year-One positions in Family Medicine and Royal College specialties that may or may not resemble the rotating internships of old. Pursuing Family Medicine training as a "two-year internship" in order to be licensed prior to entering Royal College specialty training is being highly discouraged on economic and ethical grounds. An informal survey leads one to believe that many in our class have been so discouraged: most of us who are Royal College specialty-bound are going where the money is and applying directly to Surgery, Psychiatry, Internal Medicine, Paediatrics, or whatever. This is obviously quite a change in class sentiment compared to six months ago, and should hearten those who genuinely wish Family Medicine residency positions for the purpose of becoming primary-care physicians. Hopefully, everyone will get what they want—for now.

A return to the lecture hall, after an eighteen-month-long hiatus, awaits us on November 30, 1992. I understand that this first day includes a COMPULSORY orientation session that all MUST attend—no skipping without a darn good reason. And, no, sticking around a Fiji beach for an extra day or two to study "photo-dermatology" is NOT a good enough reason. See you all there!

A look into the Meds '93 crystal ball reveals some interesting goodies in store over the next few months. Among them: internship interviews, Tachycardia, more exotic electives, CIMS Match Day (a time of great joy or great sorrow, depending on your point of view), a little quiz over two days called the MCCQE Part 1 (incorrectly referred to by many as simply "The LMCC"), and, if one is good, Graduation Day, a magical moment that will commemorate four (or five or seven) of the best years of our lives. Good luck to all, and I will keep you posted in these pages of more class developments as they unfold.

Ω

Meds '94

by Justin Amann

First of all, welcome back everybody! We all made it back after our very varied summers. Some traveled, some worked, some did electives, some watched TV. (Sean), and some got married (Caroline, Jon, Naz...congratulations! Any more volunteers - Nina?)

Some rapid fire news: Burke is having a baby, or at least that's the scuttlebutt. (Personally, I think Judy deserves some credit too.) Last week he showed the class an ultrasound of the baby Baird at 14 weeks. It was giving Dad the finger. Burke will be only the second father in the class. (Brian is already a Dad to all of us.)

Last week, two of our classmates reported a Kamyar sighting. In fact, this has been happening with increasing frequency, and renowned English UFO investigator Rory Tate predicts even greater frequency as clerkship begins.

Jon Riddell claims he met Elvis over some beers at the Grad Club. He also claims our men's hockey team is going to win the championship this year. Only one of these claims is likely correct. How many of you pick Elvis?

About a dozen of us wrote Part One of the American Board Exams back in September. A bargain at $200 to have your ego bashed in the city of your choice: Detroit, Ann Arbor, Boston or Montreal. Only Norm (my new hero) returned with tales of anything but despair.

Leila and Margherita organized a program this fall to educate high school students on the risks and benefits, hows and whys of sex. A bold move, taking frank talk about sex into high schools in London. Congratulations to you two and to all who participated.

Steve Lai (Superguy) is reported to have superhuman strength. This closet athlete is now a "beast at large" after slugging home runs in intramural baseball games and also has a contract offer to be the Dallas Cowboys' new QB (it's true!).

Oktoberfest saw more reputations fall this year.

The Meds soccer team, Team Dartos, finished the season 5-0, and is aiming for a second straight championship. Good luck in the playoffs.

During the Blue Jays' run for the World Series, study time took as big a beating as Atlanta and Oakland combined. UMEC, in a shining display of magnanimity, has agreed to lower the pass requirement for the upcoming ICC exam by 2% per playoff game watched, plus an extra 5% for anybody who drove to Toronto for game 5. Dr. Haase has been usurped by Roberto Alomar as honourary class president.Finally, clerkship is almost upon us. Psych yourselves up, it's like a real job. You gotta be there everyday! Use all the resources at your disposal. And remember: it's more than a job, it's slave labour. So enjoy it!

Ω

Meds '95

by James McNabb

Welcome back, kids. I can't tell you how thrilled I was to see everyone arrive back to school with smiling faces and refreshed minds in anticipation of what is sure to be a most exhilarating and inspirational experience in 2nd year Medicine. I'm relatively new to this article-writing thing, but, in my time away from a hectic academic schedule and volunteer work down at the mission, I have attempted to assemble a brief account of the recent events of this young school year. Please note at this time that this article is being written from the standpoint of one medical student and does not necessarily represent the opinions held or the events being partaken in by the entire Meds '95 class.

That said, I would like to extend heartfelt congratulations on behalf of the entire class to Jeff Spence and Nicole Desmarais. Nicole wed this past summer and Jeff recently witnessed the birth of his firstborn son. Best wishes also to Martin McFarlane and Donika, and to Ambrose Au and Lydia who have announced their engagements to be married. Congratulations folks! [Editor's note: Felicitations to the author and Ms. Andrea "But-we're-not-living-together" Brkovich are also in order, it's their ten month anniversary. Knock yourselves out.]

Turning now to events in which it might be considered ethically and morally correct for the whole class to participate, the first off was Disorientation Week. Apparently all went well as our volunteer staff assisted the first years in getting accustomed to their new surroundings. Although they tried, the Meds '95 crew didn't quite seem to have the ingenuity required to surpass the former year's artistic prowess in O-week T-shirts. But alas, who can be expected to top such a culinary coup in fashion? Thanks once again, Meds '94...with bacon.

The Fanshawe Picnic was next. An annual get together that generally provides entertainment of mammoth proportions. There were, however, some changes to the picnic this year, briefly: the 1st year class cheated their way to victory in the boat races against the 2nd year class instead of the traditional vice versa, D. J. music was provided instead of Rockin' Ramsay and his All Girl Orchestra, and professional bartenders were hired in order to minimize financial loss from handing out free beer to free-loading 2nd years. If only the two hired bar girls had attended those classes at bartending school where they would have been taught that kegs, unlike fine wine, need not be tapped prior to consumption in order to breathe...

Fanshawe was soon followed by war games. Although present in smaller numbers this year (thus forcing our medical heroes into battle against a squad of gun-happy weekend warriors from the Police Force instead of against one another) our platoon was able to prove victorious. The win can be attributed to many brave souls, not the least of which was an overly bunker-aggressive 3rd year (physician, heal thyself), as well as the leadership strategy and courage above and beyond the call of duty exhibited by our fearless, armed forces trained, Thomas "Magnum" Hurley. Conspicuous in their absence were the female brigades, led by Jen Green. although they were sorely missed, we did understand when we were informed they had been hired by a secret government task force in combination with the CIA and the Green Berets. Our thoughts are with you, ladies - bring home those P.O.W.s.

The last event which must be recounted is Oktoberfest. Two Murphy's Line school buses were responsible for transporting our thirsty folk to the Concordia Club in Kitchener. Thankfully, sing-songs were cut short with 47 bottles of beer remaining on the wall and, hey, the bus driver had sped up a little bit. As the evening wore on, no one was sure whether this was merely an opportunity for some guys and gals to get together for a few drinks, or a forced

impromptu version of "The Young and the Restless" by Das Führer for a few of the med school couples. Most had a great time regardless - who needs to have sex for the next month anyway? Oh, by the way, Brian Bell was successful in defending his Murphy Bus Lines Wrestling title, and, in his kind hearted manner, has decided to donate his winnings to the Oktoberfest Illegitimate Child Fund as well as to Sketchely Cleaners for Hart's jacket.

Well, I've just looked at the time, and appear to be woefully behind in my 3rd revision study schedule. Good luck to one and all during exams, and we hope to see you all at those well deserved post-exam celebrations.

Ω

Meds '96

by Jay Nathanson

So this is medical school. For an overwhelming majority of us, the year began (and for some of us, remains) as a non-stop celebration of the detoxifying marvels of the human liver. After a host of orientation activities, including a class barbecue, a party at the Graduate Club, a pub at the Rideout, a sports day in Gibbons Park, a beach day in Grand Bend, and a picnic in Fanshawe Park, we were getting acquainted with each other. Special thanks to the class of '95, and especially Britt and Jeff, for making orientation such a success.

With the commencement of classes, the revelry and merriment continued unabated. Our class was now starting to feel very comfortable together, and we met for a Star Trek season premiere party and movie nights. By the time that the Health Sciences Pub rolled around, it was hard for us to believe that we had known each other for such a short time.

Within weeks, however, we had moved on to more cerebral pursuits, and were faced with several serious medical dilemmas: Welsh-Allyn or Heine? Littman or Tycos? Every October, the instrument companies, smelling the new and not quite yet debt-ridden medical students, visit Western to elucidate on their products' distinctive features and inform us where the other brand is lacking. We could look forward to spending over six hundred dollars on various "toys" that, for the most part, will rarely be used and, when needed, can be found in abundance in any hospital. The first few weeks of classes also brought with it a very important lesson: if you're in medicine for the money, start writing textbooks.

Then we started dissections. Six medical students, dressed in (initially) white lab coats, trying to ignore the smell, exploring the wonders of human anatomy, hunched over a cadaver, engrossed in the task of finding one nerve, vessel, or node among thousands. The ultimate in bonding.

Finally, class elections were held. Jason, who had been on the campaign trail since the very first day (if not before), was elected Class President. As well, Farhan was chosen to be our Vice-President and April was elected as Treasurer.

Well, that's the way it is. I hope everyone has a great first trimester (or had a great trimester — depending on how long it takes for the Journal to come out), and I'll see you next Journal.

Ω

Feature Section

This month's Feature Section is Substance Abuse & Toxicology. Articles range from the obcure to the more general.

On page 17 is Dr. David Smith's discussion of co-presentation of chemical dependency & mental illness. Aron Ross writes about the obscure practice of toad licking (p. 31). Anne Silas and Dr. R. Gerace present the effects of cocaine toxicity (p. 39). Plus a drug research update and more!

CHEMICAL DEPENDENCY AND MENTAL ILLNESS: A PSYCHIATRIC CHALLENGE

David W. Smith, M.D.

INTRODUCTION

In the study of chemical dependency, the term "comorbidity" refers to the simultaneous occurrence of psychiatric disorders and alcohol or drug abuse disorders. Affected persons are commonly referred to as "dual-diagnosis" or "dual disorder" patients. The "Vision for the 90's" submitted to the Ontario Government highlighted the need for improved assessment and treatment of the dual-diagnosis patient. Estimates place the number of dual-diagnosis patients in the province at 250,000[9]. Review studies show that 40 percent or more of psychiatric inpatients have a chemical dependency diagnosis as well as a psychiatric diagnosis[9,10]. A recent study at the North Bay Psychiatric Hospital revealed that 56.7 percent of psychiatric inpatients satisfied the criteria for chemical dependency according the MAST [Michigan Alcohol Screening Test]. In spite of the frequency of drug abuse and drug addiction among the psychiatric patient population, most psychiatric units in general hospitals and admitting units in provincial hospitals do not routinely assess for chemical dependency, or provide structured intervention.

CASE VIGNETTE

Don B. is a 30-year-old male alcoholic. He reports that he was a slow learner in school and was labelled as a hyperactive child. He began abusing alcohol as a teenager and reports that he drank to "feel normal". From the age of 18 to 28 Don entered detoxification centres more than fifty times. He completed six alcohol treatment programs. Don was never able to remain sober for longer than six months in spite of his AA (Alcoholics Anonymous) attendance where he obtained a sponsor and worked on the 12 steps towards recovery. Don reported that he experienced rapid mood swings when sober. He reported "My mood would go from the floor to the clouds in a matter of hours." Assessment at the St. Thomas Psychiatric Hospital Addiction Unit, determined that he might be suffering from an atypical affective disorder and he was started on Lithium Carbonate. Lithium treatment has allowed Don to enjoy long-term sobriety for the first time. After two weeks of Lithium therapy he reported,"For the first time in my life I feel like an earth person."

Don B's story illustrates the tragedy of delayed diagnosis. Chemical dependency practitioners and psychiatrists must examine individuals who frequently relapse more closely in order to determine possible psychiatric disorders.

ABOUT THE AUTHOR:

Dr. David W. Smith completed his medical education and psychiatric residency at the University of California at Los Angeles. He is board certified in psychiatry by the American Board of Psychiatry. Dr. Smith has held a number of academic positions, which include: Medical Director of the St. Thomas Psychiatric Hospital's Addiction Rehabilitation Unit, Assistant Clinical Professor of Psychiatry at the University of Western Ontario, a member of the Dual Disorder Committee of the American Society of Addiction Medicine, and faculty member of The School for Addiction Studies of the Addiction Research Foundation.

IMPEDIMENTS TO PROPER ADDICTION ASSESSMENT

Historically, drug addiction was not felt to be a distinct disorder. Until 1968, diagnostic nosologies did not allow for a separate addiction diagnosis classifying alcohol addiction and drug addiction as subtypes of sociopathic personality disorders[7]. In spite of diagnostic clarification of addictive disorders in the DSM-III-R, practitioners continued to believe that treatment of a patient's mental disorder would automatically cure the chemical dependency. The professional community now realizes that each disorder requires treatment.

Chemical dependency education was not a part of the curriculum of many medical schools until quite recently. University psychiatric departments have typically involved themselves in chemical dependency research. Psychoanalytic thinking continues to interfere with the understanding of the disease of chemical dependency. In addition to being better trained in assessment techniques, physicians need to become aware of the importance of the self- help community. AA,NA[narcotics anonymous] Alanon and Adult Children of Alcoholics groups are critical to recovery.

Diagnosis of a psychiatric disorder based solely upon the presenting symptomatology[12] occurs too often in the mental health field. Physicians commonly review the outside psychiatric records of

patients admitted to an addiction unit and to note numerous psychiatric symptoms which lack documentation of the temporal relationship between the symptoms and drug or alcohol use. Alcohol and drug histories are absent from many files. Patients are diagnosed incorrectly and given antidepressant medication or antipsychotic medication unnecessarily.

IMPEDIMENTS TO PROPER MENTAL HEALTH ASSESSMENT

In addition to impediments in the assessment of addiction, negative attitudes and lack of information have prevented addiction professionals from making adequate mental health assessments. Addiction treatment professionals are frequently in recovery themselves, and tend to promote the form of treatment that was helpful for them. This usually involves a strong 12-step AA/NA approach. Although a strict 12-step approach is critical with some patients, the dual-disorder patient has caused the addiction treatment community to become more flexible in its approach. For example, the addiction field has had to re-examine its commonly-held belief that all drugs are bad drugs. AA has clearly stated its position in a 1984 publication entitled "The AA Member-Medication and other Drugs"[Alcoholics Anonymous 1984; [9]]. The pamphlet states;"It becomes clear that just as it is wrong to enable or support any alcoholic to become re-addicted to any drug, it's equally wrong to deprive any alcoholic of medication which can alleviate or control other disabling physical and/or emotional problems."[13].

Addiction professionals must understand that a relapse to chemical dependency may not be the result of the patient's failure to "Work the program." In the case of the dual disorder patient, a relapse to chemical dependency could result from a relapse of the patient's mental illness. Failure to attend self help groups should not always be seen as a resistance to recovery from chemical dependency. For example, many months may be needed for a patient with a generalized anxiety disorder with panic to feel comfortable in a group setting. Given the heterogeneity of the dual-disorder population, individualized treatment planning is essentia[14]. Traditionally, individualized treatment planning was frowned upon and was seen as evidence of the patient attempting to manipulate the addiction treatment system. There are still treatment programs where individual sessions are discouraged. Patients suffering from Post-traumatic Stress Disorder from incest, or patients with panic disorder, are unlikely to talk about their experiences in a group until they are at ease individually. The dual-disorder patient generally does poorly in a treatment setting that places the same expectations upon on all patients.

PRACTICAL APPROACHES TO ASSESSMENT

Before making a psychiatric diagnosis on a patient with a chemical dependency an understanding of the following principles: the acute, chronic and withdrawal effects of the patient's drug or drugs of choice; common symptoms of protracted withdrawal, and the stage of recovery that the patient is in. Most studies suggest that drug abuse does not cause major mental illness [excluding drug induced mental disorders], but either exacerbates it or hastens its onset[11].

An accurate psychiatric diagnosis cannot be made while the patient is under the influence of alcohol or tests positive for illicit drugs in the urine or blood. Serious consideration of a psychiatric diagnosis should not be undertaken for at least two to four weeks after detoxification. If the psychiatric symptoms worsen in spite of abstinence, it would be more likely that an underlying psychiatric illness is present.

Gorski has described the recovery process from chemical dependency in stages[6]. The pretreatment phase is characterized by the patient denial of the presence of addiction. Unless there is a documented period of abstinence during which psychiatric symptoms were present, a psychiatric diagnosis during this period is inappropriate. Detoxification or stabilization is marked by psychiatric and physical symptoms induced by drug or alcohol withdrawa[18]. Withdrawal from alcohol, stimulants, sedative/hypnotics, marijuana or opiates produce unique mental status changes that mimic major mental illness.

Alcohol withdrawal can cause agitation, visual hallucinations and severe depression. The agitation and hallucinations should cease by the end of the first week of abstinence; depression, however, can persist for weeks. If the depression worsens beyond the two to four week period, treatment of the patient with antidepressant medication may be necessary.

Stimulant withdrawal, [i.e., cocaine and amphetamines] produces depression, lethargy, insomnia and occasionally a paranoid psychosis. The paranoia induced by cocaine rarely lasts longer than forty-eight hours, whereas it may last for several weeks in the case of amphetamines. Urine screening is beneficial in clarifying the etiology of a paranoid psychosis.

Sedative/hypnotic withdrawal produces agitation, irritability, insomnia, emotional lability

and depression. The syndrome of protracted abstinence is particularly evident in sedative/hypnotic withdrawal[14]. Protracted abstinence is a central nervous system abnormality characterized by neural hyperexcitability, altered thyroid function, poor visual spatial perception and central neurochemical receptor alterations. Protracted abstinence can last for weeks to months after the acute withdrawal has ceased. Clinically, protracted withdrawal is evidenced by insomnia, anxiety, depression, memory disturbances and irritability. Although this syndrome has been associated with all addictive substances, it seems to be most pronounced with alcohol and sedative/hypnotics. Symptoms of protracted withdrawal are frequently episodic whereas the symptoms of an emerging mental illness are consistent and persistent.

Opiate withdrawal produces agitation, restlessness, insomnia, depression and emotional lability. Withdrawal from cannabis can produce a similar syndrome however the symptoms are less pronounced. Unique to marijuana is the prolonged time that it is stored in body fat. In chronic cannabis smokers the withdrawal period could last for four to six weeks[15].

The next stages of recovery are early, middle, and late. Early recovery is marked by a strong focus on relapse prevention and adapting to a sober lifestyle. Depressions are common during this period as patients take inventory of the effects that addictive chemicals have had on their lives. These depressions, however, are frequently situational. Middle recovery is characterized by the development of a balanced lifestyle. Late recovery is characterized by development of healthy self esteem, personal growth and healthy living.

TREATMENT ISSUES

The most common psychiatric diagnoses coexisting with a diagnosis of addiction are schizophrenia, affective disorders, post-traumatic stress disorder, generalized anxiety disorder and antisocial personality disorder. These disorders cannot be successfully treated if the patient is using mind- altering chemicals.

SCHIZOPHRENIA

In my experience of working with patients with schizophrenia, two unique issues emerge. Patients with schizophrenia enjoy the positive atmosphere recovering in the community. There is an expectation of recovery that does not exist in most mental health settings. This sometimes causes patients to want to shed the mental illness label and stop their antipsychotic medication. Patients must then be educated about their illness. Additionally, with respect to sobriety and recovery, patients become more aware of uncomfortable side-effects from antipsychotic medication. Clinicians should be sensitive to this problem and be willing to make reasonable adjustments in dosage.

AFFECTIVE DISORDERS

A common problem encountered in this group of patients is trying to convince them that medications for affective disorders (antidepressants or Lithium Carbonate) do not produce physical dependence. Twenty-five percent of alcoholics suffer from major affective disorders[8]. Studies reveal that comorbid depression predicts poor vocational functioning, more substance use, and greater dysfunction.

GENERALIZED ANXIETY DISORDER

Ten to twenty percent of alcoholics suffer from a generalized anxiety disorder[8]. Typical patients with alcohol dependence and generalized anxiety disorder develop alcoholism as a byproduct of their attempt to ease anxiety. Practitioners must be aware of the extreme physical discomfort these individuals' experience during recovery. Pharmacological treatments, along with behavioral interventions, are thought to be the most effective. As stated previously, these individuals will require a lot of time before they will participate in group discussions. Patients with generalized anxiety disorder may do best in individual addiction intervention and treatment.

POST-TRAUMATIC STRESS DISORDER

Symptoms of Post-traumatic stress disorder frequently appear spontaneously as recovery progresses. Most addiction specialists suggest waiting for several months before engaging the patient in ''uncovering psychotherapy.'' The patient with Post-traumatic stress Disorder is an exception. If the patient is experiencing flashbacks of the incest perpetrator, nightmares, severe emotional lability, depression, and anxiety, to a degree that causes them to be dysfunctional, then therapy should not be postponed. Depending upon their symptomatology, patients may require antidepressants and psychotherapy. Recovery support groups can be most helpful with these individuals. If the patient is female, she may not feel comfortable in mixed AA/NA groups and may prefer to attend Women For Sobriety meetings.

ANTISOCIAL PERSONALITY DISORDER

A patient who presents for addiction treatment with a diagnosis of Antisocial Personality Disorder should be carefully reviewed for accuracy of diagnosis. Knowing whether the antisocial disorder predated the chemical dependency or occurred as a result of it is important. Antisocial Personality Disorder has been found to be present in four percent of males and less than one percent of females in the general population. Among alcohol abusers, however, the incidence increases to fifteen percent of males and ten percent of females7. Longitudinally, the diagnosis has been shown to be unreliable[7]. MMPI [Minnesota Multiphasic Personality Inventory] abnormalities frequently return to normal in this patient population after long-term sobriety. The therapist must be careful not to allow his or her anger with the patient to prompt a non-therapeutic decision to be made. Many patients demonstrating Antisocial Personality have been victims of severe child abuse resulting in them having frequent conflicts with authority figures. Clear therapeutic contracts with these patients which contain the therapist's expectations regarding attendance at counselling sessions, self help groups and drug testing is critical. In instances where there is unresolved anger, depression or trauma concerning childhood issues, individual psychotherapy may be indicated.

SUMMARY

Patients with a dual-disorder of chemical dependency and major mental illness represent a challenge to the treatment philosophies of the fields of mental health and addiction. An understanding of each area is essentia[14]. Without the development of an integrated approach to the treatment of this patient population, unnecessary delays in diagnosis and treatment will continue to occur, resulting in unnecessary suffering.

REFERENCES

1. Martin, G. Treating Alcohol and Drug Problems in Ontario; A Vision for the 90's. Advisory Committee On Drug Treatment. pp. 164-166 (1990).
2. Group For The Advancement Of Psychiatry, Committee On Alcoholism and the Addictions. Substance Abuse Disorders: A Psychiatric Priority. *American Journal of Psychiatry* **148:**1291-1299 (1991).
3. Shuckit M. The History of Psychotic Symptoms in Alcoholics. *J. Clin. Psychiatry* **43:**53-57 (1982).
4. Minkoff K. An Integrated Treatment Model for Dual Diagnosis of Psychosis and Addiction. *Hosp. and Community Psychiatry.* **40:**1031-1036 (1989).
5. Miller N.S. Psychiatric Diagnosis in Alcohol and Drug Dependence. *Annals of Clinical Psychiatry,* **3:**79-89 (1990).
6. Gorski T. Staying Sober, Herald House—Independence Press. pp. 39-128 (1986).
7. Blume S.B. Dual Diagnosis: Psychoactive Substance Dependence and Personality Disorders. *J. Psychoactive Drugs.* **21:**139-144 (1989).
8. National Institute on Drug Abuse. State of the Science Report. Rockville M.D. The Institute, Psychiatric Issues In Addiction Medicine. 1990 reprinted in American Society of Addiction Medicine, Review sourse syllabus, 1990.
9. Cooper G., Kent C. Special needs particular populations; dual disorders. In: Alcohol and Drug Problems; A Practical Guide For Counsellors (Howard B.A. & Lightfoot L., Eds.) Toronto: Addiction Research Foundation, 1990 [in press].
10. Ries R. Substance Abuse Intervention on Inpatient Psychiatry. *Substance Abuse* **10:** 28-32 (1989).
11. Turner W.M., Impact of Substance Abuse on the Course and Outcome of Schizophrenia. *Schizophrenia Bull.* **16:**87-95 (1990).
12. Wallen M.C. Impediments to Effective Treatment of the Dually Diagnosed Patient. *J. Psychoactive Drugs.* **31:**161-168 (1989).
13. Alcoholics Anonymous. The AA Member-Medication and Other Drugs. New York; Alcoholics Anonymous World Services, 1984.
14. Geller A. Protracted Abstinence. *Review Syllabus, American Society of Addiction Medicine* pp. 195-202 (1990).
15. Schwartz R.H. Marijuana: An overview. *Paediatric Clinics of North America* **34:**305-317 (1987).

Ω

CALIFORNIA SUBSTANCE ABUSE PROGRAM

Dennis Zander, Meds'94 & Ross Mantle, Meds '95

The five day "Professional in Residence Experiential Program" offered at the world famous Betty Ford Center in Palm Springs California was the beginning of a new approach to substance abuse for both of us this summer. The centre was founded in 1982 by Mrs. Ford, former First Lady of the United States. She was also a former alcoholic and drug addict. Based on her experiences in a US Navy treatment program, Mrs. Ford was inspired to create a new way of treating civilian substance abusers outside of the hospital. Since 1982, 14,000 individuals have graduated from the program and the Center has become recognized worldwide. The trendy Palm Springs location and $11,000 (US) price tag for a one month stay have made this desert enclave the subject of much National Enquirer lore, since Elizabeth Taylor and other well known Hollywood figures have been admitted over the years. In fact, the cost of treatment at the Center is in the lower half of the price range available for similar programs across the United States. Further, less than 1% of clients are celebrities. In addition, $250,000 (US) in financial aid is available each year to those in need.

"Betty Ford"

For the alcoholic or addict, both inpatient and outpatient options are available. A comprehensive aftercare program following admission and a family program which takes place during the patient's stay are standard and included in the fee. The Center strongly encourages the families of substance abusers to become involved in family rehabilitation to decrease the likelihood of relapse upon return of the abuser to the home environment.

The four week inpatient program is highly structured with therapeutic activities planned from 6 AM to 10 PM every day. The patients' schedules include group therapy, art therapy, chores, exercises, lectures, Alcoholics Anonymous (AA) meetings, meditation, and some time for socializing. The inpatient centre consists of three single sex units and one mixed unit with twenty beds in each. As part of an attempt to keep patients focused on treatment, diversions such as novels, musical instruments, electronic devices, clothes, telephone conversations, or other diversions are either not allowed or kept to a bare minimum. Also, residents are not allowed to socialize with patients in other units. Dress and conduct codes are conservative and enforced with threat of dismissal. Despite the restrictions on individual freedoms and activities within the Center, the doors are not locked and any patient may leave at any time and receive a partial refund. Nevertheless, the large number of rules create a certain "us and them" sentiment among the patients which contributes to their camaraderie and is a constant source of sardonic humour. New patients are continuously introduced to the unit as graduates are discharged. Newcomers are therefore able to witness other patients in their unit at all stages of recovery and can gain inspiration from those preparing to go home. Importantly, the senior "inmates", as they sometimes call themselves, also gain self esteem from helping newer patients adjust to the "system."

The outpatient program is identical to the inpatient program except that patients return home in the evenings instead of staying in the unit. As well, the cost is less. The cost of both the inpatient and outpatient programs include flight arrangements and hotel accommodation for one family member in the week-long family treatment program. Additional family members are encouraged to attend, but must pay for their own expenses. The family program attempts to provide close relatives insight and therapy into their family member's (and perhaps their own) addiction. Since patients' families are usually dysfunctional, either resulting in or from the patient's addiction, the Center encourages extersive aftercare.

A unique feature of the Center is the "Professional in Residence" program. The program is an opportunity to learn about the Center and to actually participate in treatment for 5 days. The Center provides a travel stipend and free accommodation through donations and grants designed to promote "Aunt Betty's" treatment philosophy. Police officers, doctors, college athletics coaches, teachers, as well as medical students (the largest contingent) participate. Admission to the medical student program is fairly competitive; less than one in eight applicants are accepted. This summer, four groups of sixteen medical students were invited. In each session, eight students participated in the inpatient program while the other eight were involved with the family program. Schools from all over the United States and Canada were represented.

Our days began at 6 am with a short bus ride from the Howard Johnson's Hotel where all the medical students stayed free of charge. Although we were exceedingly well-briefed beforehand, no one was spared the anxiety of stepping into an unfamiliar family group or onto units inhabited by twenty strangers with severe addiction problems. Would we be accepted or perceived as intruders? I recall watching the emotions on the face of the first woman I met change from surprise to embarrassment as she shuffled along the hall still "coming down", her hair dishe-veled, and her movements unsteady. Oddly, by the end of the afternoon this lady and I were becoming friends. She had a quick wit and a warm smile. She also had a long series of purple marks on the medial surfaces of her forearms where she had injected heroin. Most of us in the program quickly realized that this was not

the time to play junior doctor. We were there to learn from them, not the reverse, and they knew it.

A typical day began with a thirty minute meditation walk around the Center and breakfast with the patients. Morning activities involved exercise (everyone participates, no exceptions), lectures, and group therapy. Departure to each activity was preceded by a call to "circle". In circle we recited the Serenity Prayer ("God grant me the serenity to accept the things I cannot change..."), joined hands and chanted the unit chant ("North Hall, we stand tall, no more drugs or alcohol..."). Three lectures each day were designed to provide the patients with insight into their addiction and ranged from the pharmacology of abuse, to spirituality, to family dynamics and self-esteem. The lectures were of a consistently high calibre and were often extremely inspirational and entertaining. In addition to these activities medical students attended lectures on the behind-the-scenes workings of the Center.

Group therapy can be intensely emotional and personal—this was definitely one of the highlights of the program for us. While patients occasionally greeted our presence in "group" with mistrust, most of us were quickly accepted and actually encouraged to participate.

Activities related to the AA Twelve-Step program, upon which treatment at Betty Ford is based, are carried out in the afternoons. The first five steps take place at the Center and the remainder are executed after discharge. Aocoholics Anonymolus meetings, which may also include graduates from the centre and members of the community, are held on the campus in the evenings.

For the medical students, there were more memorable times waiting each night around the hotel hot tub as we sat and soaked, reflecting on the day. Comparing notes, we found that without exception, every student experienced a bond to the patients they were in contact with. We also realized the unfortunately high relapse rate after a single course of treatment. According to veteran therapists at the Center, there is no way to predict an individual's long-term sobriety.

The Betty Ford Center staff, approximately eighty-percent of whom are recovering themselves, put on an unforgettable training program for us. We feel that the experience was extremely valuable to us. The interpersonal skills we refined will assist us in all areas of medicine.

Addicted and alcoholic persons have a message, and perhaps a lesson, for those willing to listen.

Ω

Applications to attend the Betty Ford summer training course may be obtained by writing to :

Betty Ford Centre,
Training Department,
3900 Bob Hope Drive
Mairape, Ca 922702

THE POTENTIAL VALUE OF PSYCHEDELIC DRUGS: THE MPTP AND MDMA STORIES

Jeffrey Poltisky, Meds '94.

INTRODUCTION

Hallucinogenic agents have a long history of being prepared to create altered states of mind. This history may even predate ethnologic records of these agents (see article by Aron Ross in this issue). Ethnologically, hallucinogens have been prepared from natural sources and used for ceremonia[1], religious, and medicinal purposes. A recent trend in the use of mind-altering substances involves chemical synthesis of psychedelic drugs for recreational use—the so-called "designer drugs." In addition to their recreational use, psychedelic drugs are also used therapeutically and investigationally. The synthesis of psychedelic agents is based on legitimate pharmaceutical research, and has resulted in the production of a variety of mind altering substances, each with an interesting history.

The two major classes of designer drugs are synthetic phenylethylamines (mescaline analogs) and synthetic opioid derivatives. This paper presents a discussion of two psychedelic drugs: 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine (MPTP), a derivative of meperidine synthesis, and N-methyl-3,4-methylene-dioxyamphetamine (MDMA), a mescaline analog. MPTP is used in the development of animal models designed to further understand the pathologic basis of Parkinson's Disease. MDMA has potential therapeutic value in the treatment of patients who exhibit psychological disturbances.

MPTP (1-METHYL-4-PHENYL-1,2,5,6-TETRA-HYDROPYRIDINE)

MPTP, a known neurotoxin, was discovered as a result of a bizarre detective story. In the late 1970's, a 23-year-old chemistry graduate student in Berkeley, California spontaneously developed severe Parkinsonian-like signs and symptoms that lasted 18 months. Autopsy revealed selective degeneration of the substantia nigra, thus supporting the diagnosis of Parkinsonism1. Further research by scientists from the National Institute of Mental Health (Bethesda, Maryland) showed that the subject was a drug addict and had been synthesizing meperidine analogs for illicit sale. Analysis of chemical samples obtained from the student's basement laboratory revealed MPTP as a contaminant. Subsequent to this event of sudden death, investigators identified several young adults in northern California who presented with virtually identical clinical signs[2,3]. The facts that these individuals were also drug addicts and that the second outbreak also occurred in northern California led investigators to suspect a toxic contaminant. Indeed, drug samples analyzed from an illegal laboratory showed MPTP to be the likely toxin[2,3]. These clinical observations prompted pharmacologists and clinicians to probe the physiologic, pharmacological, and toxicological aspects of the chemical intermediate MPTP.

PHYSIOLOGIC EFFECTS IN HUMANS

In 1983, Langston and coworkers reported on four drug addicts who had been ingesting the synthetic heroin MPPP[2]. These addicts had been producing MPPP in a clandestine basement laboratory. Each subject presented with signs and symptoms remarkably similar to Parkinson's Disease (PD); the presentation of these subjects was thought to be due to contamination of drug samples with MPTP. In 1985, the same group reported on seven human cases of known MPTP-toxicity, in which each patient was diagnosed with clinically significant signs of the Parkinsonian state[3].

The subjects studied self-administered, by intravenous injection, MPPP in amounts ranging from 4.5 grams (g) over four days to 30 g over 20 days. The frequency of administration ranged from 3-10 injections per day[3]. Biochemical, haematologic, urologic, radiologic, and neurologic studies were non-contributory in all subjects. Each subject manifested clinical symptoms with acute and chronic components. The following signs were associated with the acute component. Intravenous

administration resulted in a burning sensation in each subject. Subjects all felt typical heroin-like euphoria or dreaminess along with illusions, hallucinations, and blurred vision. Motor disturbances included sudden distal limb jerkiness and bradykinesia. Eventually, bradykinesia predominated and was accompanied by slow, dysarthric speech and intermittent resting tremor. Four of the seven subjects reported being "frozen" by three days post-administration. The chronic stage of MPTP neurotoxicity developed in days to weeks and consisted of most of the cardinal signs and symptoms of PD. These signs and symptoms included bradykinesia, rigidity, tremor, cog-wheeling, micrographia, masked facies, widened palpebral fissures, glabellar sign, hypophonia, odynophagia, seborrhea, and diaphoresis[3].

Combination therapy of carbidopa/levidopa dramatically improved the extrapyramidal symptoms of most subjects. Symptoms, however, returned if therapy was discontinued. Moreover, increasing doses of carbidopa and levidopa were necessary to suppress clinical signs[3].

PHARMACOLOGICAL PARAMETERS

After MPTP is administered to primates, it rapidly disappears from all tissues except the eye[4], and produces no detectable basic, acidic, or neutral metabolites in organic extracts of biological tissues. Within one hour, large amounts of the highly water-soluble 1-methyl-4-phenylpyridinium (MPP+) ion is detectable in peripheral tissues and in the central nervous system (CNS)[4-6]. In contrast to the rapid disappearance of MPTP, MPP+ (half-life, 48-100 hours) is extremely long-lasting in the primate brain. Further, while MPP+ concentrations begin to decline in most brain regions and throughout the body between 24 and 72 hours after administration, MPP+ levels are actually increasing in the substantia nigra[7]. Metabolism of MPTP to MPP+ takes place via a two-step oxidation process with the production of 1-methyl-4-phenyl-2,3-dihydropyridinium (MPDP+) ion. Evidence suggests that this reaction is mediated primarily by monoamine oxidase (MAO)-B[8-12]. This ion may be an important intermediary toward achieving significant CNS concentrations of MPP+. For example, some observations suggest that MPP+ does not cross the blood brain barrier (BBB) and must be injected directly into the CNS[13-15]. This concept contradicts various animal models designed to study the effects of MPTP. These studies employ i.v. injections of MPTP. Perhaps i.v. injections result in significant CNS concentrations because MPTP is converted to MPDP+ which first crosses the BBB and is then converted into MPP+.

NEUROTOXICOLOGIC PARAMETERS

Injection of MPP+ into the striatum, medial forebrain bundle, or substantia nigra of rats resulted in marked striatal dopamine (DA) depletion[13-15]. MPTP-induced dopamine depletion has also been

reported in mouse substantia nigra, nucleus accumbens, and olfactory tubercle[3,16,17]. Although MPTP has been effective in producing dopamine depletion, actual neuronal cell loss has proved more difficult to produce. To date, primates remain the only animal that develops the major clinical signs of a full-blown and enduring extrapyramidal syndrome analogous to that seen in idiopathic PD[18]. MPTP causes similarly selective and extensive destruction of neurons of the substantia nigra par compacta (SNpc) and the locus coeruleus in primate brain[19].

This species variability may exist because of the fact that whereas MPP+ disappears quickly from rodent brain, MPP+ is the predominant metabolite retained in primate brain for long periods. These differences may relate to inherent differences in response of cells to MPTP and its metabolites. Rodent liver and brain cells metabolize MPTP and MPP+ quickly; primate cells are much more sensitive to these toxins[20].

Other neurochemical changes which occur in primate brain tissue include reductions in acid metabolites of dopamine, norepinephrine, and serotonin in the medulla, pons, midbrain, hypothalamus, putamen, caudate, and frontal cortex[21].

CLINICAL SIGNIFICANCE: THE LINK BETWEEN MPTP AND PD

Parkinson's Disease is a neuropathological disorder characterized by degenerative changes in neurons in the SNpc and consequential reductions in striatal DA content[22]. In addition to the SNpc, pathologic changes in idiopathic PD also include the locus coeruleus and the hypothalamus[22]. These brain regions also contain high densities of binding sites for MPTP[23]; this localization of binding sites establishes a potential link between MPTP neurotoxicity and idiopathic PD. Both conditions present clinically with akinesia, rigidity, and tremor.

Pervading theories regarding causation of PD include genetic factors, CNS aging, and foreign agents (microorganisms and toxins). Barbeau and co-workers have suggested that the pathologic mechanisms of PD may be associated with exposure to environmental factors or endogenous toxins in genetically predisposed individuals subject to the normal processes of aging[20]. One such potential toxin is MPP+.

The primary clinical relevance of MPTP is based on the accumulation of MPP+ in the SNpc[7,24]. Knowledge of this anatomic selectivity prompted investigators to utilize MPTP and MPP+ as substances which could induce clinically significant Parkinsonian symptoms in animal models. This research was expected to expand scientific understanding of the underlying neuropathologic mechanisms of MPTP-induced Parkinsonism and of idiopathic PD. Although a number of plausible theories have arisen to explain these mechanisms, the pathologic basis of PD or drug-induced Parkinsonism is still unknown.

One theory which does have credence, however, relates to SN iron stores. The "Iron Hypothesis" is based on the fact that basal ganglia structures are rich in iron[25]. In the presence of ferrous iron, MPTP forms superoxide ions and oxidizes DA[26,27]. Thus, basal ganglia iron stores may contribute to the mechanism of MPTP neurotoxicity. Iron stores also appear to play a role in idiopathic PD; autopsied brain tissue from patients with clinically diagnosed idiopathic PD revealed elevated concentrations of SN iron[26]. The putative role of iron in MPTP-mediated neurotoxicity and in idiopathic PD provides indirect support for the theory that pyridine analogues are involved in the underlying pathology of PD.

As well as being used to explain the pathologic basis of disease, animal models may also be used to screen drugs designed to treat disease. Murine and monkey models of PD have been employed for this purpose. Tatton and co-workers have utilized a murine model of MPTP-induced Parkinsonism to detect the value of drugs which slow progression of dopaminergic striatal neuronal degeneration[27]. Research by this group has shown that the MAO inhibitor deprenyl prevents the death of toxically damaged neurons. The mechanism of action may not involve blockade of conversion of MPTP to MPP+. Another group has found that the MPTP monkey model is useful for predicting the potential value of new anti-Parkinson's drugs[28]. Levodopa, a DA agonist used to treat PD, frequently causes dyskinesia, the long term side effect of therapy. These researchers are using an MPTP monkey model to study the long term effects of potential anti-Parkinsonian drugs, with the hope that a drug will be found that does not produce dyskinesias.

MDMA (N-METHYL-3,4-METHYLENEDIOXY-AMPHETAMINE)

MDMA is a methoxylated amphetamine base that was first synthesized in 1912. MDMA is derived from materials which contain a methlenedioxyphenyl ring, such as isosafrole, safrole, piperonal, and peiperonylactone. The D-stereoisomer of MDMA is quantitatively more potent at exerting its effects than the L-isomer[29]. MDMA has many code names, including ecstasy, XTC, E, Adam, and Eve. This hallucinogen has been available on the illicit drug market since 1968.

The drug's popularity grew throughout the 1970's and 1980's and since the drug enforcement agency (DEA) placed MDMA on Schedule 1 of the Controlled Substance Act in 1985, MDMA has gained even more prominence[30].

PSYCHOLOGIC AND PHYSIOLOGIC EFFECTS

Subjects taking MDMA report a sense of "closeness" in the first few hours after ingestion[31]. Various physiologic effects also occur and include tachycardia, dry mouth, tremor, palpitations, diaphoresis, parasthesias, trismus, and bruxism. Whereas many people report an increased alertness, many people also report a decreased ability to concentrate. A minority of subjects also report visual, but not auditory, hallucinations. These hallucinations tended to occur in the peripheral and not the central visual field[31].

Twenty four hours after ingestion, subjects tended to feel drowsy. This drowsiness is likely associated with the insomnia of the previous 24 hours. Muscle aches, fatigue, depression, difficulty concentrating, and headache were also experienced. The worst subjective sensations however, were a sense of anxiety, worry, fear, and irritability 24-hours post-ingestion[31]. About one half of MDMA users report that the positive effects of the drug diminished with repeated administration, whereas the negative effects tended to become more profound.

NEUROPHARMACOLOGY

Rat brain regions affected by MDMA include the cerebral cortex, basal ganglia, septal area, thalamus, epithalamus, hypothalamus, hippocampus, and midbrain[32]. The pharmacologic profile of MDMA at various CNS receptor and uptake sites is: 5-HT uptake > alpha2 adrenergic = 5-HT2 = M1 (muscarinic) = H1 (histaminic) > norepinephrine uptake = M2 = alpha1 adrenergic = beta adrenergic > DA uptake = 5-HT1 >> DA D2 > DA D132. Studies of the effects of MDMA on rat brain shoed that the dopaminergic and serotonergic systems are significantly affected by MDMA. MDMA has been shown to decrease levels of tryptophan hydroxylase (TPH), serotonin (5-HT), and 5-hydroxy-indole acetic acid (5-HIAA) in several brain regions[33,34]. As well, effects on serotonergic system are much more pronounced and longer lasting than on dopaminergic neurons[35]. Dopamine appears to be crucial for MDMA to exert its effects on serotonergic neurons, since haloperidol blocks the effects of repeated doses of MDMA. Further, deinnervation of SN DA neurons with 6-hydroxy dopamine (6-OHDA) prevented the decrease in TPH levels in rat neostriatum compared with non-treated brain regions such as the frontal cortex and hippocampus[36]. Finally, both DA and 5-HT uptake blockers (amfonelic acid and fluoxetine, respectively) also block MDMA-induced decreases in TPH levels[37,38].

MDMA TOXICITY

MDMA toxicity has been studied on a variety of animal models. For example, doses which cause death in 50% of subjects tested (LD50) range from 32 mg/kg in rat, to 14 mg/kg in dogs, and 22 mg/kg in monkey39. Lethal doses in man may only be inferred from various sources of literature, and the values vary. Levels near 1 µg/ml have been associated with fatalities40, whereas levels as high as 7 µg/ml have not[41].

Therapeutic or recreational uptake of MDMA usually involves oral doses in the range of 75-100 mg. At this level, a variety of side effects may occur which include tachycardia, tremor, facial muscle contracture, diaphoresis, nausea, vomiting, and bruxism. Disturbances become more severe as dosage is increased. Impaired cognitive, sensory, and motor skills have also been observed[30,31].

Brain regions that suffer the greatest extent of MDMA-induced neurotoxicity also exhibit dramatic reductions in 5-HT uptake sites. For example, cortical regions that showed the most extensive destruction by autoradiographic analysis included the prefrontal, anterior cingulate, entorhinal, and parietal cortical regions[32]. These changes occurred as early as 18 hours after a four-day treatment regimen of 20 mg/kg MDMA (b.i.d.). The caudate-putamen regions, thalamus, and hippocampus also showed early degenerative changes[32]. In the midbrain, regions with 5-HT projections (such as the terminals and axons of the SN) were more dramatically disturbed than regions with 5-HT uptake sites (i.e. perikarya) such as the raphe nucleus, central gray, ventral tegmental area, and pontine reticular formation[32].

The severity and extent of MDMA-induced lesions depend highly on the dose and frequency of administration. Neurotoxic effects may persist up to one year before structural recovery may occur; functional impairment can be permanent.

Human deaths associated with MDMA may be direct or indirect. Direct deaths due to high doses may be due to overwhelming neurologic involvement, with a special risk for people with underlying cardiovascular disease. Indirect deaths, which seem to be more common, are likely due to the effects of cognitive, sensory, and motor impairment induced by MDMA—for example, a motor vehicle accident. As well, many people who have died with significant blood levels of MDMA have also had trace or significant blood levels of other drugs such as alcohol, cocaine, lysergic acid diethylamide (LSD), dextromethorphan, acetaminophen, and others. Thus, attributing death to MDMA is difficult not only on the basis of the effect of the drug itself, but also on the predisposition of the user[42].

CLINICAL USE OF MDMA

MDMA was first used psychotherapeutically in the late 1970's (before the drug was placed in Schedule 1 by the DEA) for patients who exhibited addictive behaviors. MDMA appeared to have the ability to assist the patient in surrendering his will to a "Higher Power" for personal guidance toward ultimate achievement of self-control. This attitude is thought to be critical in aiding the patient to gain release from previously destructive addictive behaviors, relations, and beliefs. One other important aspect in the therapeutic use of MDMA (and other psychedelic drugs) is the patient's understanding that the therapist has undergone MDMA training sessions and is capable of appreciating the subjective effects of the drug[43].

Patients who are acceptable candidates for MDMA psychotherapy should fulfill the following criteria: they should not have peripheral vascular or cardiovascular disease, they should not be on psychotropic medication, they should not have metabolic disturbances or liver disease, and they should not be pregnant[43]. Further, such patients should be relatively well-adjusted people with a willingness to solve their problems.

The patient should also be instructed of all potential benefits and risks of the drug so that the patient may give informed consent for the session. The benefits include enhanced communication, introspection, and elevated mood. The physiological risks are associated with the sympathomimetic side effects of MDMA (bruxism, tachycardia, nausea, vomiting, hypertension) and with the potential 5-HT depletion and neurotoxicity based on animal studies. The psychological side effects relate to the breakdown of the patient's defense mechanisms; the pain of incompletely reconciled grief or previous traumatic experiences may be felt both psychologically and somatically. Symptoms that may occur include psychologic depression and anxiety as well as headaches and dyspnea[43]. Side effects are not known to last beyond one to two days, whereas the duration of potential benefit from a successful session may be immeasurable.

The entire therapeutic session may last may hours. After taking the drug, patients initially spend some time in isolation either in silence, meditation, or prayer waiting for the drug to take effect. Patients may continue to spend time alone in introspection once the drug begins to exert its effects. Once the patient feels confident with the individual issues and various physical signs, the patient is encouraged to confront these issues with the therapist. An additional 50 mg dose of MDMA may be offered to extend the effects of the drug.

Once the session is over and the drug effects begin to wear off, the patient may want to discuss the entire episode in earnest with the therapist[43].

Greer and Tolbert found that about 90% of patients had positive and beneficial experiences with MDMA[44]. These researchers concluded, based on various clinical encounters, that MDMA serves to reduce emotional stress and fear associated with perceived threats to one's psychological integrity[44]. Exactly how MDMA achieves this loss of fear is unknown. Nonetheless, patients gain access to unresolved conflicts from childhood and other past relations and feel as though they have gained a broader, more complete understanding of themselves and their relations with others[44].

Currently, psychotherapeutic applications of MDMA is legal only in Switzerland. Recent reports, however, suggest that the Food and Drug Administration (FDA) may lift the existing ban on research employing LSD and MDMA[45]. The Swiss group of Widmer and colleagues use MDMA to study human consciousness[47]. Treatment of selected patients consists of two to four treatment sessions per year with MDMA or other psychoactive substances. Widmer's group have not observed any addictions MDMA. Further, addictions to alcohol, medical drugs, heroin, and other agents have been greatly reduced by MDMA-supported psychotherapy46. No evidence has accumulated to substantiate suspected CNS toxicity due to MDMA in the therapeutic dose range[46].

The current restriction on the therapeutic use of psychoactive substances suggests that these agents have not received the necessary scientific credentials to make this type of therapy acceptable. The lack of scientific support, coupled with negative social attitudes toward the use of psychoactive agents for medical treatment, make the likelihood of government-supported research a distant possibility. Only knowledge (gained from studies similar to those by Greer and Tolbert, and by Widmer et al.) may change this trend from rejection to acceptance.

CONCLUSION

Psychedelic drugs continue to be preferred agents among drug users to create altered states of mind. MPTP and MDMA are only two examples of a number of chemical compounds that have arisen as a result of psychedelic drug synthesis. Clearly, uncontrolled use of these agents can produce profound toxic effects in humans with disastrous results. In a controlled environment, however, each agent has a potential scientific benefit. Further research with MPTP may assist scientists not only to elucidate the underlying mechanisms of PD, but to develop improved treatment modalities for this disease as well. Further, controlled therapeutic trials with MDMA may prove this agent to be a useful adjunct in the treatment of addictive disorders and psychological disturbances.

The current surge in interest in MPTP, MDMA, and other such chemicals for the treatment and study of neurodegenerative, addictive, and psychological disorders suggests that hallucinogens and their byproducts will play an important role in the progression of scientific knowledge.

REFERENCES

1. Davis G.C., et al. Chronic Parkinsonism secondary to intravenous injections of meperidine analogues. *Psychiat. Res.* **1**:249-54 (1979).
2. Langston J.W., et al. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. *Science.* **219**:979-80 (1983).
3. Ballard P.A., Tetrud J.W., & Langston J.W. Permanent human Parkinsonism due to 1-methyl-4-1,2,3,6-tetrahydropyridine (MPTP): Seven cases. *Neruology.* **35**:949-56 (1985).
4. Langston J.W., et al. MPP^+: Identification of a metabolite of MPTP, a toxin selective to the substantia nigra. *Neurosci. Lett.* **48**:87-92 (1984).
5. Markey S.P., et al. Intraneuronal generation of pyridinium metabolite may cause drug-induced Parkinsonism. *Nature.* **311**:464-67 (1984).
6. Melamed E., et al. Mesolimbic dopaminergic neurons are not spared by MPTP neurotoxicity in mice. *Eur. J. Pharmocol.* **114**:97-100 (1985).
7. Irwin I. & Langston J.W. Current Concepts: II. Selective accumulation of MPP^+ in the substantia nigra: A key to neurotoxicity. *Life Sci.* **36**:207-12 (1985).
8. Kulkarni S.K. & Mehta A.K. MPTP: A neurotoxin relevant to the pathophysiology of Parkinson's disease. *Neurology.* **11**:384-86 (1986).
9. Chiba K., et al. Metabolism of the neurotoxic tertiary amine, MPTP, by brain MAO. *Biochem. Biophys. Res. Commun.* **120**:574-78 (1984).
10. Heikkila R.E., et al. Protection against the dopaminergic neurotoxicity of MPTP by MAO inhibitors. *Nature.* **311**:467-79 (1984).
11. Heikkila R.E., et al. Current Concepts: IV. Dopaminergic neurotoxicity of MPTP in the mouse: relationships between MAO, MPTP metabolism and neurotoxicity. *Life Sci.* **36**:231-36 (1985).
12. Cohen G. & Mytilineou C. Current Concepts: VII. Studies on the mechanism of action of MPTP. *Life Sci.* **36**:231-36 (1985).
13. Bradbury A.J., et al. MPP^+ is neurotoxic to the nigrostriatal dopamine pathway. *Nature.* **319**:56-7 (1986).
14. Sayre L.M. Biochemical mechanism of action of the dopaminergic neurotoxin MPTP. *Toxicol. Lett.* **48**:121-49 (1989).
15. Heikkila R.E., et al. Dopaminergic neurotoxicity of MPTP in mice. *Science.* **49**:135-40 (1985).
16. Lewin R. Age factors loom in Parkinsonism research. *Science.* **234**:1200-1 (1986).
17. Gupta M., et al. MPTP alters monoamine levels in systems other than the nigrostriatal dopaminergic system in mice. In: MPTP: A Neurotoxin Producing a Parkinsonian Syndrome. (Markey S.P. et al., Eds.) New York: Academic Press. pp. 1957-59 (1986).
18. Chiueh C.C., et al. Current Concepts: III. Primate model of Parkinsonism: Selective lesion of nigrostriatal neurons by MPTP produces an extrapyramidal syndrome in Rhesus monkeys. *Life Sci.* **36**:213-18 (1985).
19. Seniuk N.A., Tatton W.G., & Greenwood C.E. Dose-dependent destruction of the coeruleus-cortical and nigral-striatal projections by MPTP. *Brain Res.* **527**:7-20 (1990).
20. Barbeau A., et al. Ecogenetics of Parkinson's disease: 4-hydroxylation of debrisoguine. *Lancet* . **ii**:1213-16 (1985).
21. Fuller R.W. & Steranka L.C. Current Concepts: VIII. Central and peripheral catecholamine depletion by MPTP in rodents. *Life Sci.* **36**:243-47 (1985).

22. McGeer P.L., McGeer E.C., & Suzuki J.S. Aging and extrapyramidal functions. *Arch. Neurol.* **34:**33-35 (1977).
23. Sandyk R. & Iacono R.P. The neurotoxicity of MPTP and its relationship to the pathophysiology of Parkinson's disease. *Int. J. Neurosci.* **44:**165-67 (1989).
24. Snyder S.H. & D'Amato R.J. MPTP: A neurotoxin relevant to the pathophysiology of Parkinson's disease. *Neurology.* **36:**250-58 (1986).
25. Riederer P., et al. Transition metal, ferritin, glutathione, and ascorbic acid in Parkinsonian brains. *J. Neurochem.* **52:**515-20 (1989).
26. Sofic E., et al. Selective increase of iron in substantia nigra zona compacta of Parkinsonian brains. *J. Neurochem.* **56:**978-82 (1991).
27. Tatton W.G. et al. Interactions between MPTP-induced and age-related neuronal death in a murine model of Parkinson's disease. *Can. J. Neurol. Sci.* **19 (suppl. 1):**124-33 (1992).
28. Bedard P.J., et al. Levodopa-induced dyskinesia: Facts and fancy. What does the MPTP monkey model tell us? *Can. J. Neurol. Sci.* **19 (suppl. 1):**134-37 (1992).
29. Schmidt C.J. & Taylor W.L. Neurochemical effects of methylenedioxyamphetamine in the rat: Acute versus long-term changes. In: Ecstasy: The Clinical, Parmacological, and Neurotoxicological Effects of the Drug MDMA. (Peroutka S.J., Ed.). Boston: Kluwer Academic Publishers. pp. 151-69 (1990).
30. Seigel R.K. MDMA: Nonmedical use and intoxication. *J. Psychoactive Drugs.* **18:**349-54 (1986).
31. Downing J. The psychological and psysiological side effects of MDMA in normal volunteers. *J. Psychoactive Drugs.* **18:**335-40 (1986).
32. Battaglia G., Zaczek R., & DeSouza E.B. MDMA effects in brain: Pharmacologic profile and evidence of neurotoxicity from neurochemical and autoradiographic studies. In: Ecstasy: The Clinical, Pharmacological, and Neurotoxicological Effects of the Drug MDMA. (Peroutka S.J., Ed.) Boston: Kluwer Academic Publishers. pp. 171-99 (1990).
33. Harvey J.A., McMaster S.E., & Fuller R.W. Comparison between the neurotoxic and serotonin depleting effects of various halogenated derivatives of amphetamine in the rat. *J. Pharmacol. Exp. Ther.* **205:**581-89 (1977).
34. Bakhit C. & Gibb J.W. Methamphetamine-induced depression of tryptophan hydroxylase: Recovery following acute treatment. *Eur. J. Pharmacol.* **76:**229-33 (1981).
35. Schmidt C.J. & Taylor V.L. Direct central effects of acute methylenedioxy methamphetamine on serotonergic neurons. *Eur. J. Pharmacol.* **156:**121-31 (1988).
36. Sekerke H.J., et al. Correlation between brain levels and biochemical effects on the optical isomers of *p*-chloroamphetamine. *J. Pharmacol. Exp. Ther.* **193:**835-44 (1975).
37. Hotchkiss A.J. & Gibb J.W. Long-term effects of multiple doses of methamphetamine on tryptophan hydroxylase and tyrosine hydroxylase activity in rat brain. *J. Pharmacol. Exp. Ther.* **214:**257-62 (1980).
38. Schmidt C.J., Wu L., & Lovenberg W. Methylenedioxymethamphetamine: A potentially neurotoxic amphetamine analogue. *Eur. J. Pharmacol.* **124:**175-78 (1986).
39. Hardman H.F., Haavik C.O., & Seevers M.H. Relationship of the structure of mescaline and seven analogs to toxicity and behavior in five species of lab animals. *Toxicol. Appl. Pharmacol.* **25:**299-309 (1973).
40. Dowling G.P., McDonough III, E.T., & Bost R.O. "Eve" and "Ecstasy:" A report of five deaths associated with the use of MDEA and MDMA. *JAMA.* **257:**1615-17 (1987).
41. Brown C. & Osterloh J. Multiple severe complications from recreational ingestion of MDMA (Ecstasy). *JAMA.* **258:**780-81 (1987).
42. Dowling G.P. Human deaths and toxic reactions attributed to MDMA and MDEA. In: Ecstasy: The Clinical, Pharmacological, and Neurotoxicological Effects of the Drug MDMA. (Peroutka S.J., Ed.). Boston: Kluwer Academic Publishers. pp.63-75 (1990).
43. Greer G.R. & Tolbert R. The therapeutic use of MDMA. In: Ecstasy: The Clinical, Pharmacological, and Neurotoxicological Effects of the Drug MDMA. (Peroutka S.J., Ed.). Boston: Kluwer Academic Publishers. pp. 21-55 (1990).
44. Greer G.R. & Tolbert R. Subjective reports of the effects of MDMA in a clinical setting. *J. Psychoactive Drugs.* **18:**319-27 (1986).
45. Pekkanen S. San Francisco Examiner. p.1. July 27, 1992.
46. Widmer S. Clinical work using MDMA in Switzerland since 1985. *MAPS Newsletter.* **3:**13 (1992).

Ω

BUFOTENINE AND THE "TOAD LICKING" PHENOMENON: HISTORICAL PERSPECTIVES AND CURRENT TRENDS

Aron D. Ross

INTRODUCTION

The ritual use of bufotenine as a hallucinogenic drug has long been practiced within some South American tribal cultures, but until recently, its use among North American drug users was virtually unknown. In the last few years, bufotenine has become the subject of media controversy when street-drug users were reported to have ingested bufotenine-containing toad venom for its alleged hallucinogenic effects; the media dubbed this practice "toad-licking". These reports have revived interest in the hallucinogenic properties of bufotenine, but to date very few thorough accounts of the current toad licking phenomenon have been published. Although this curious practice is not likely to become a widespread drug abuse problem, it does merit a detailed examination.

HISTORICAL PERSPECTIVES AND ETHNOPHARMACOLOGY

Bufotenine is a hallucinogenic alkaloid found in several species of toads, plants and fungi. Bufotenine is the principal plant alkaloid from the seeds of Anadenanthera (Fig. 1), a genus of leguminous trees consisting of the two species A. peregrina and A. colubrina. Tribal groups of South America use these species to prepare a hallucinogenic snuff powder which they consume. The earliest record of snuff prepared from A. peregrina is likely from 1496, when Europeans observed Taino Indians of Hispaniola self-administering the snuff by nasal insufflation through a long bamboo tube. This snuff was reported to produce a rapid hallucinogenic effect and was primarily used in magicoreligious ceremonies[19]. Similar snuffs, called yopo, cohoba or paricà, made from the ground seeds of A. peregrina, were (and may still be) used by various tribal groups native to British Guyana, Brazil, and the Upper Orinoco Valley region of Venezuela and Colombia. The closely related species A. colubrina is found in the snuffs known as vilca or hulica in Southern Peru and Bolivia, and cèbil in Northern Argentina. Each Indian tribe prepares the snuff in a slightly different manner but generally the seeds are toasted and ground into a powder which is mixed with lime from crushed snail shells or ash from the bark of certain trees. The powder is then sniffed through a tube made of wood or bird bone2. The alkaline plant ash and lime are thought to act not only as binding agents, but to facilitate the diffusion of alkaloids through the nasal mucosa as well. A typical 5 gram dose of yopo snuff is taken up to three times a day and produces a rapid intoxication, of 15-120 minutes duration characterized by initial stimulation, excitement, and hallucinations followed by a hypnotic or unconscious state. As well as bufotenine, Anadenanthera seeds also contain lesser amounts of two chemically related hallucinogenic alkaloids, dimethyl tryptamine (DMT) and 5-methoxy-DMT, both of which may contribute to the hallucinogenic properties of Anadenanthera snuffs.

Figure # 1

In addtion to plant species, bufotenine is also contained in the toxic secretions of the cane toad (Bufo marinus) and the Colorado River or Sonoran desert toad (Bufo alvarius). The cane toad is found in South and Central America, the Southern United States, Puerto Rico, Hawaii, and Australia, In response to provocative stimuli, the toad secretes a milky white venom from the parotid glands. This venom serves as a very effective natural defense against predators since, in addition to bufotenine, the toad venom also contains potentially lethal quantities of digitalis-like cardiac glycosides[16]. Archaeological findings of large quantities of Bufo

ABOUT THE AUTHOR:

Aron Ross is currently enrolled in a PhD program in Pharmacology at the University of Toronto. Mr Ross has also obtained B.Sc and M.Sc degrees in Pharmacology (University of Toronto).

skeletal remains from the ancient Olmec ceremonial site of San Lorenzo, Veracruz (1200-900 B.C.) suggest that the Olmec had knowledge of the properties of cane toad venom and may have used it as a "fortifier" in fermented ritual beverages[19]. Preparations of cane toad venom are still in use by a few indigenous tribal healers in Veracruz, Mexico, who use techniques passed down for generations to process and detoxify the venom, which is rolled into pills for later uses, for example, as an aphrodisiac[5].

Along with plants and toads, bufotenine has been isolated from certain species of fungi. Small amounts of bufotenine have been found in hallucinogenic mushrooms of the genus Amanita[1]. The psychotropic properties of that species, however, are more likely due to the presence of the two principal alkaloids ibotenic acid and muscimol[18]. Interestingly, literary references have often associated mushrooms with toads, as for example the use of the word "toadstool" to describe certain toxic mushrooms. Similar chemical relations of certain hallucinogenic toad and mushroom species may have been known long before these associations could be validated scientifically.

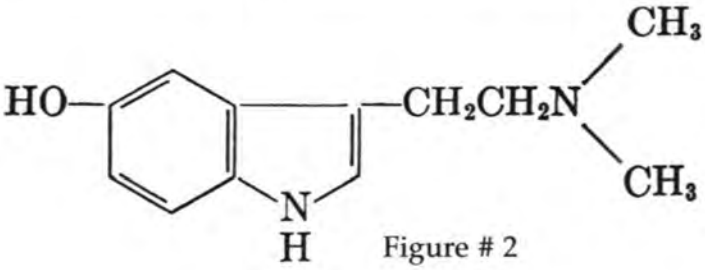


Figure # 2

PHARMACOLOGY OF BUFOTENINE

Bufotenine, also known as 5-hydroxy-N,N-dimethyltryptamine (5-OH-DMT) and dimethyl serotonin, is a serotonin homologue which is closely related structurally to the hallucinogenic alkaloids DMT and 5-methoxy-DMT (Fig. 2). Bufotenine was first synthesized in the 1930's. Over two decades later, in 1956, the pharmacological effects of bufotenine in humans were first reported[4]. In a study by Faber and Hawkins, intravenous (IV) doses of bufotenine (4-16mg) were administered to four inmates at the Ohio State Penitentiary. The subjects experienced dose-dependent psychological effects including vivid colour hallucinations, mental confusion, and feelings of euphoria and depersonalization. The physiologic effects noted were mydriasis, nystagmus, parasthesias, burning mouth, chest pain and dyspnea, nausea, vomiting,and purpling of the face and neck. The purple colour was described as "the approximate hue of an eggplant" and was thought to be due to serotonin-induced bronchiolar constriction and consequent hypoxemia. One subject's subjective experience with the drug was described in the following way: "He saw red spots passing before his eyes and red purple spots on the floor, and the floor seemed very close to his face. Within two minutes the visual phenomena were gone but they were replaced by a yellow haze". The psychologic effects, which are reminiscent of side effects caused by LSD and mescaline, developed rapidly and disappeared completely within 7-60 minutes, in a dose-dependent fashion. A subsequent study reported similar effects from intramuscular (IM) injections of bufotenine at doses of 10-15 mg, but no observable effect was noted when bufotenine was given intranasally at a dose of 14 mg or orally at doses of up to 100 mg. The inefficiency of oral dosing is likely due to the extensive first-pass metabolism by monoamine oxidase[3]. Pharmacokinetic studies have found that IV bufotenine is very rapidly absorbed from the blood and excreted in the urine, predominantly (70%) in the form of the metabolite 5-HIAA. Roughly 4% can be recovered from the urine in the unchanged form[11]. The toxicity of bufotenine in humans is not well known. Certain toxic responses, however, have been observed. An intra-muscular (IM) injection of 40 mg of bufotenine produced tachycardia, auricular fibrillations and extreme cyanosis in one patient[20] and resulted in the development of cardiac arrhythmias of the nature of multiple ectopic beats from supraventricular foci, at IV doses of 10-15 mg[3]. The pharmacological and toxicologic mechanisms underlying the behavioral effects of bufotenine have not yet been extensively studied, but there is evidence to suggest that its action as a partial agonist at serotonergic 5-HT2 receptors is involved[10].

CURRENT TRENDS: "TOAD LICKING"

For the past several years reports have circulated of a new trend in the use of bufotenine as a street drug - in the form of "toad licking" - the practice of ingesting the hallucinogenic secretions of the cane toad. This bizarre new practice caused something of a media sensation; exaggerated accounts of toad licking appeared in news reports throughout North America where toad licking was often referred to as the "latest fad". Media attention to the toad licking phenomenon seems to have begun shortly after the release of a critically acclaimed 1987 comic documentary Cane Toads by Australian film-maker Mark Lewis. The film dealt with the colourful history of the cane toad in Australia and alluded to the possibilities of

ingesting toad venom for its hallucinogenic effect. Both the film and toad-licking received major press coverage in newspapers and magazines throughout North America, with articles appearing in Newsweek[24], The New York Times[9], Scientific American[8], Smithsonian[13] and Medical Post[21], and various local newspapers. Doubt exists as to whether toad licking was ever practiced among North American drug users prior to the media reports that drew attention to the hallucinogenic possibilities of toad venom. Contrary to what the sheer volume of reports would indicate, toad licking is still a rare occurrence. At least four incidents of deliberate toad venom ingestion have been documented, all of which resulted in hospitalization. In New Mexico, two teenagers ingested cane toad venom after reading news reports of the "fad", and had to be hospitalized[8]. Further, in Australia, deaths have been reported as a result of ingesting cane toad eggs[13] and after drinking tea brewed from cane toad venom[23]. Media publicity was again an instigating factor when two Toronto men, aged 28 and 31, ingested cane toad secretions within a few days after watching a CBC-TV screening of Lewis' film Cane Toads[6,14,15]. One of the two men had to be treated in the intensive care unit at North York General Hospital for seizures. One of the most thoroughly documented cases of intentional cane toad venom ingestion was reported by a pediatrician who treated a 10 year old boy admitted to the emergency ward at a Florida hospital[17]. Upon admission, the boy was experiencing acute episodes of incoherence and complained of severe headaches and hallucinations. Electrocardiographic findings revealed secondary atrioventricular block (type I). No other clinical findings were significant. The boy was given i.v. fluids and monitored overnight. The next day both his behavior and electrocardiogram had returned to normal and he later admitted that he and his friends had been licking cane toads for the purpose of "acting crazy".

The most prominent clinical features of cane toad poisoning consist of profound drooling, seizure activity, arrhythmias, and cyanosis. Treatment for bufotenine intoxication is based upon supportive and symptomatic measures. Recommended drug therapy can include activated charcoal, hydrocortisone sodium succinate for respiratory complications, phenobarbital to control seizure activity, phenoxybenzamine (an a-receptor blocker) to relieve hypertension, and propranolol (a ß-blocker) to reverse cardiac arrhythmias[12,7].

LEGAL STATUS

Bufotenine is not available by prescription anywhere in the world nor does there appear to be an illicit market for the synthesized drug. In the United States bufotenine is covered under Schedule I of the Controlled Substances Act (the same schedule that covers highly addictive drugs such as cocaine and heroin) since there is the potential for abuse and no known medical uses for bufotenine. Rumours about a bill to ban toad licking in Georgia were later reported to be false[23], but other sources mention that such a bill is under consideration in South Carolina[17]. The government of Queensland, Australia has restricted the use of Bufo secretions by classifying them as dangerous substances under its Drug Misuse Act[22]. In Canada, toad-licking is not illegal, according to a quote from a Toronto police constable, and cane toads are sold legally at several pet stores[15].

CONCLUSIONS

Ingestion of toad venom and bufotenine is still a relatively rare and isolated occurrence among North American street-drug users. However, with continued media attention to the hallucinogenic possibilities of these agents, further incidents involving cane toads or other bufotenine containing substances may be anticipated. Considering the likelihood of serious injury as a consequence of toad venom ingestion, medical clinicians should be aware of this phenomenon and attempt to monitor the emergence of this drug abuse trend in the future.

REFERENCES

1. Chilton W.S., Bigwood J. & Jensen R.E. Psilocin, bufotenine and serotonin: Historical and biosynthetic observations. *J Psychedelic Drugs* 11:61-69 (1979).
2. deSmet P.A.G.M. A multidisciplinary overview of intoxicating snuff rituals in the Western hemisphere. *J Ethnopharmacol* 13:3-49 (1985).
3. deSmet P.A.G.M. & Rivier L. Intoxicating snuffs of the Venezuelan Piaroa Indians. *J Psychoactive Drugs* 17:93-103 (1985).
4. Fabing H.D. & Hawkins J.R. Intravenous bufotenine injection in the human being. *Science* 123:886-887 (1956).
5. Furst P.T. *Hallucinogens and Culture*. Chandler and Sharp series in cross cultural themes. Novato, Chandler and Sharp Publishers (1976).
6. Harris C. Beware the poisonous cane toad. *The Globe & Mail*: July 31 (1990).
7. Hitt M. & Ettinger D.D. Toad toxicity. *New Engl J Med* 314:1517-1518 (1986).
8. Horgan J. Bufo abuse: A toxic toad gets licked, boiled, teed up and tanned. *Sci Am* 263:26-27 (1990).
9. Maslin J. Australian 'toads' and 'feathers'. *The New York Times*, March 21, C15 (1988).
10. McClue S.J., Braziell C. & Stahl S.M. Hallucinogenic drugs are partial agonists of the human platelet shape change response. A physiological model of the 5-HT2 receptor. *Biol Psychiatry* 26:297-302 (1989).
11. McLeod W.R. & Sitaram B.R. Bufotenine reconsidered. *Acta Pychiatr Scand* 72:447-450 (1985).
12. Oeheme F.W., Brown J.F. & Fowler M.E. Toxins of animal origin. *In*: Doull J., Klaassen C.D. & Amdur M.O. (eds.) *Toxicology: The Basic Science of Poisons, 2nd ed.* Toronto, MacMillan Publishers, pp. 557-577 (1980).
13. Park E. Way down under, it's revenge of the (yech!) cane toads. *Smithsonian 21(7)*:138-145 (1990).
14. Priest L. Man who licked toad poison given anti-convulsion drugs. *The Toronto Star* July 31:A2 (1990).
15. Pulling N. Licking Toad puts men in hospital *The Globe & Mail* July 30:A1-A2 (1990).
16. Radford D.J., Gillies A.D., Hinds J.A. & Duffy P. Naturally occurring cardiac glycosides. *Med J Austr* 144:540-544 (1986).
17. Ragonesi D.L. The boy who was all hopped up. *Contemp Pediatrics* 7:91-94 (1990).
18. Ray O. & Ksir C. *Drugs, Society and Human Behavior*. St. Louis/Toronto/Boston, Times Mirror/Moseby Publications (1990).
19. Schultes R.E. An overview of hallucinogens in Western culture. *In*: Furst P.T. (ed.) *Flesh of the Gods: The Ritual Use of Hallucinogens in Western Culture*. New York/Washington, Praeger Publishers, pp. 3-54 (1972).
20. Turner W.J. & Merlis S. Effect of some indolealkylamines on man. *AMA Arch Neurol Psychiatry* 73:1251-1254 (1959).
21. Weber S. Tell those tempted to taste a toad: "Better beware in case you croak". *Medical Post* 26(29):2/50 (1990).
22. Anonymous. Frog Crime. *The Journal* 19(11):2 (1990).
23. Anonymous. Toad legend takes a licking. *Montreal Gazette* February 22:A9 (1990).
24. Anonymous. "Can't lick 'em? Then smoke 'em. *Newsweek* June 15:63 (1992).

Ω

PSYCHEDELIC DRUG RESEARCH UPDATE

THE HOASCA PROJECT: PROPOSAL FOR A BIOMEDICAL INVESTIGATION OF AYAHUASCA

Dennis J. McKenna, Ph.D.

Ayahuasca is a Quechua term meaning "vine of the souls," and is one of the numerous indigenous names for the hallucinogenic drink prepared from a combination of two Amazonian plants, Banisteriopsis caapi, and Psychotria viridis. In Amazonian Peru and parts of Colombia and Ecuador, the drink is known as ayahuasca; in other parts of the Amazon, it is known as yage, natema, or pilde; in Brazil, it is known as hoasca, or sometimes simply "the tea." In whatever cultural context it is found, and by whatever name, ayahuasca plays a pivotal role both in the spiritual life of the populations that use it, and in local ethnomedical practices. The drink is regarded as both a sacrament, and a medicine. For the shamans familiar with its properties, it is both a diagnostic aid and a respected teacher; for the patients who seek the healing the shamans can offer, it is the ideal holistic medicine, providing the means to cleanse and heal both the mind and the body. From the perspective of modern psychopharmacology, practically nothing is known of how it actually affects the human mind/body.

Recently, a unique opportunity has become available to carry out a biomedical investigation of the immediate and long-term effects of ayahuasca in human users. This opportunity has resulted from recent friendships established by the author with members of a Brazilian organization, the Unao do Vegetal (UDV) which is essentially a syncretic religious movement in which the collective, periodic ingestion of hoasca tea is the central ceremony and sacrament. Unlike the more traditional use of ayahuasca in the context of mestizo or aboriginal shamanism, the use of hoasca tea within the UDV is strictly regarded as a religious or spiritual practice (as opposed to a curing or medical practice). Moreover, many of the younger adherents to the UDV "cult" tend to be well-educated urban professionals. Some of the members are Western-trained physicians, psychiatrists, or other health professionals who frequently possess a solid training in medical disciplines and a healthy scientific curiosity about the physical and psychological effects of hoasca tea. They understand as much as anyone does about the active alkaloids found in hoasca tea, and about its putative mechanism of action. Many of these individuals would like to learn all that can be learned about how it works, but at the same time they maintain a sense of reverence regarding their sacrament; they consider that an effort to understand hoasca using the tools and paradigms of science is not a sacrilege if it is pursued as part of a sincere effort to increase our knowledge of this remarkable medicine.

This enlightened attitude establishes an intellectual climate in which a pharmacological and psychological investigation of hoasca could be carried out if the required resources were available. While attending a conference on the biomedical aspects of hoasca which was hosted by the UDV in Sao Paulo in June, 1991, I made a proposal for a biomedical investigation of the human pharmacology of hoasca to some of the leaders of the UDV. The response was more than receptive, it was enthusiastic. Since this conference, we have remained in frequent contact, and have continued to work together on developing a proposal setting forth the objectives

These articltes were reprinted with the kind permission of Rick Doblin, president of MAPS. *(See page 38.)*

and methodologies for a pilot study on the action of hoasca in humans.

As currently conceived, a number of parameters related to the psychophysiological effects of hoasca will be investigated, among them the following:

Composition of hoasca teas. The UDV recognizes several kinds of hoasca, which differ in their modes of preparation and in their effects. The composition and amount of active alkaloids in these various types of tea will be analyzed and compared.

Acute pharmacokinetics of hoasca. Pharmacokinetics is the study of the absorption, metabolism, and excretion of drugs. The phar-macokinetics of the major alkaloids of hoasca (harmine and DMT) will be determined in blood samples taken from volunteers using a technique known as gas chromatography/mass spectrometry (GC/MS).

Acute/long-term effects of hoasca on serotonergic functions. Hoasca, like other hal-lucinogens, is known to interact primarily with receptors for the neurotransmitter serotonin (5-HT, 5-hydroxytryptamine). The effects of hoasca on serotonergic functions can be determined in blood and plasma samples by analyzing various parameters, such as the levels of hormones known to be modulated by the serotonin system (e.g. prolactin, ACTH, beta-endorphin). In addition, blood platelets contain many of the same serotonin receptors that are found in the brain, and psychopharmacologists have long used platelet receptor binding assays as a peripheral marker for changes presumably occurring in the central nervous system. We propose to use platelets to monitor the effects of hoasca on certain serotonin receptor subtypes, and also to measure peripheral monoamine oxidase (MAO) inhibition. These parameters will be measured in volunteers drawn from the members of the UDV before and after the ingestion of known doses of hoasca tea.

In addition, a parallel study will investigate the possible long-term effects of hoasca by examining these parameters in a group of older maestres - members of the UDV who have taken hoasca regularly for much of their adult lives.This group of maestres will be compared with a set of age-matched control volunteers who have not taken hoasca.

These are the primary objectives of the initial study. Additional parameters may also be measured, such as the effect of hoasca on immune functions, or its effect on cognitive function as measured by psychological and cognitive assessment procedures.

Ω

[Editor's note: At the time this article was reprinted, the required $50 000 to commence research was already acquired.]

IBOGAINE UPDATE

by Bob Sisko

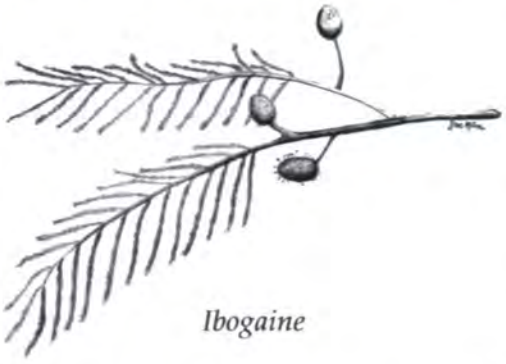
Last year, the Medications Development Division (MDD) of the National Institute on Drug Abuse (NIDA) began a research initiative to evaluate the use of ibogaine as an anti-addiction agent. Since than, numerous articles have appeared in scientific journals, both in the US and abroad, which show promising results.

Spearheading the research efforts are the Pharmacology and Toxicology Department of Albany Medical collefe, headed by Dr. Stanley D. Glick. His department published no fewer than six papers in little over a year. Other New york research institutions evaluating ibogaine include the Nathan S. Kline Institute for Psychiatric Research, a facility of the New York State Office of Mental Health affiliated with NYU Medical Center, and the City University of New York Medical School.

Claims that ibogaine is effective as atreatment for both cocaine and opiate narcotics were at first widely viewed with skepticism. Cocaine is, after all, a stimulant while opiate narcotics have an oposite effect, that of sedating the user. What they do share in common, however, is that use of either substance increases dopaminergic (DA) activity in the brain's mesolimbic system, and/or mesocortical pathways. This triggers the reward mechanism, which is associated with the reinforcing effects of

drugs of abuse. Researchers thus began looking at the relationship of ibogaine to the DA system.

In early 1991, Dr. Broderick of CUNY Medical School submitted an abstract to the College on Problems of Drug Dependence (CPDD), The African Alkaloid, Ibogaine, Alters Cocaine-Induced Accumbens Dopamine Neurotransmission: In Vivo Voltametric Studies in the Conscious Brain. She reported that ibogaine reduced cocaine induced DA increases, but without complete depletion, and observed, "These data have clinical implications because pharmacotherapeutic medications which decrease DA neurotansmission without a complete DA block could dirdumvent the reported anhedonia often associated with some cocaine treatment modalities." Her final report, presented at the CPDD's 53rd annual scientific meeting, concludes, "Thus, ibogaine's effects are consistent with current views regarding rational strategies for cocaine treatment."[1]



Ibogaine

At the same time, researchers at the Division of Neurochemistry at the Nathan Kline Institute in Orangeburg, NY were examining the relationship between ibogaine and cocaine in mice. Henry Sershen, et,al., reported this year tha[1] Ibogaine Antagonizes Cocaine-Induced Locomotor Stimulation in Mice[2]. "The results," he states, "suggest that ibogaine may have induced a selective change in the dopaminergic system that results in a decrease in responsiveness to cocaine that persisted for at least one week." He further concluded that "The above results are not in conflict with the proposed uses of ibogaine in the treatment of cocaine abuse, since increased dopamine neurotransmission has been shown to be associated with the locomotor-stimulant and reinforcing effects of cocaine. Attenuation of these effects by ibogaine could possibly reduce the craving for cocaine."

Additional work involving ibogaine and cocaine was accomplished by m.R. Dzolic, of Erasmus University in Rotterdam. An abstract submitted to the CPDD, Effects of Ibogaine on Cocaine Self-Administration in Rats, showed promising results, and compared favorably to uncontrolled clinical observations. "All this is encouraging," said Dzolic, "since it supports the idea that ibogaine is a potential long lasting interrupter of both cocaine and morphine dependency."

In June, 1992, Dzolic made and oral presentation to the CPDD at the 54th annual scientific meeting in Keystone, Colorado. The significance of his findings are twofold. Firstly, heretofore the interruption of cocaine self-administration with a non-toxic substance was unheard of. In a number of widely-reported studies, animals, when given the ability to self-administer cocaine did so continuously, ignoring food, water, and sex until they died. Secondly, Dzolic's findings are consistent with those of S.D. Glick, et.al., Effects and Aftereffects of Ibogaine on Morphine Self-Administration in Rats.[3]

Glick found that not only would ibogaine interrupt morphine self-administration, but that it continued to do so long after the ibogaine was eliminated from the body. Citing two US patents (4,499,096; 4,587,243) which describe the potential effecacy of ibogaine in treating opeate and cocaine addiction, Glick concludes, "Though far from addressing the full extent of the claims presented in the patents, the results of this study suggest that such claims should be taken seriously, and that further investigation is warranted."

In a study entitled, Interactions between Ibogaine, a Potential Anti-Addictive Agent, and Morphine: An In Vivo Microdialysis Study[4] I.M. Maisonneuve et.al. found that "It appears that ibogaine affects brain DA systems for a period of time that exceeds its elimination from the body, and during this time, alters the responses of these systems to morphine. By preventing the increase in dopaminergic transmission induced by morphine in the nucleus accumbens, ibogaine may decrease the reinforcing efficacy of morphine. Thus, although a definitive mechanism underlying the claims regarding ibogaine's therapeutic effects cannot be specified yet, the results of the preesnt study indicate that such mechanissms merit investigation."

Maisonneuve and Glick published two other papers addressing the dopamine question, Interactions between Ibogaine and Cocaine in Rats: An In Vivo Microdialysis and Motor Behavior[5]; and Acute and Prolonged Effects of Ibogaine on Brain Dopamine Metabolism and Morphine-Induced Locomotor Activity[6].

Glick then turned his attention to another claim; the claim that ibogaine will suppress the multiple symptoms of narcotic withdrawal. The claim that ibogaine attenuated many, but not all, symptoms of withdrawal was first reported by Djolic et.al., Effect of Ibogaine on Naloxone-Precipitated Withdrawal of Chronic Morphine Dependent Rats[7] Two years later, Aceto, Bowman and Harris at the Medical College of Virginia reported that ibogaine suppressed

withdrawal signs in morphine dependent monkeys[8]. A controversy was created when Sharpe and Jaffe refuted those findings, stating that ibogaine failed to reduce the majority of withdrawal in morphine dependent rats. However, Sharpe and Jaffe conceded that such discrepancies were possibly the result of methodological differences. "Despite all these differences," observed Glick, "some aspect of the opiate withdrawal symptom was ameliorated in all three studies."

Glick prepared a study to re-examine the possibility that ibogaine might attenuate morphine withdrawal. His results indicate that ibogaine significantly decreased the intensity of many withdrawal signs[9]. "Exactly how ibogaine might attenuate opiate witdrawal is, at this point, open to conjecture," Glick states. "Regardless of the explanation," he concludes, "the present results indicate that the potential usefulness of ibogaine in treating acute manifestations of opioid dependence should be further investigated."

REFERENCES

1. NIDA Research Monograph Series. **119**:285 (1992).
2. Sershen H, et.al. Ibogaine Antagonizes Cocaine-Induced Locomotor Stimulation in Mice. *Life Sci.* **50:**.1079-1086 (1992).
3. Glick SD, et.al. Effects and Aftereffects of Ibogaine on Morphine Self-Administration in Rats. European Journal of Pharmacology, **195**:341-345 (1991).
4. Maisonneuve IM, et.al. Interactions between Ibogaine, a Potential Anti-Addictive Agent, and Morphine: An In Vivo Microdialysis Study. *Eur. J. Pharmacol.* **199**:35-42 (1991).
5. Maisonneuve IM and Glick SD. Interactions between Ibogaine and Cocaine in Rats: An In Vivo Microdialysis and Motor Behavior. *Eur. J. Pharmacol* .**212**:263-266 (1992).
6. Maisonneuve IM and Glick SD. Acute and Prolonged Effects of Ibogaine on Brain Dopamine Metabolism and Morphine-Induced Locomotor Activity. *Brain Res.* **575**:68-73 (1992).
7. Djolic et.al. *Effect of Ibogaine on Naloxone-Precipitated Withdrawal of Chronic Morphine Dependent Rats. Arch Int.Pharmacodyn* **294**:64-70 (1988).
8. NIDA Research Monograph **95**:578 (1990).
9. Glick SD. Effects of Ibogaine on Acute Signs of Morphine Withdrawal in Rats: Independence from Tremor. *Neuro-pharmacol.* **31**:497-500 (1992).

Ω

MAPS (Multi-disciplinary Association for Psychedelic Studies) is a membership-based organization working to assist psychedelic research around the world to design, conduct, and report psychedelic drug studies, and to obtain government approval for this research.

For more information about **MAPS**, write to:

Rick Doblin, President
MAPS
1801 Tippah Avenue
Charlotte, N.C., U.S.A.
28205

Phone: (704)-358-9830 Fax:(704)-358-1650

THE CARDIOVASCULAR AND NEUROLOGICAL EFFECTS OF COCAINE TOXICITY

Anne Silas, Meds 94 & Rocco Gerace, M.D.

ABSTRACT

The widespread use of cocaine has led to an increase in Emergency Department admissions for treatment of the acute toxic effects of this drug. Recently, an increase in fatalities has been ascribed to its cardiovascular and neurologic complications[1]. These include acute myocardial injury, arrhythmias, stroke, seizure, and death[2]. Recognition of the cocaine abuser's presentation in the ED, and knowledge of the various applicable treatments, may reduce mortality and morbidity associated with cocaine intoxication.

INTRODUCTION

Cocaine is a naturally occurring alkaloid of the Coca plant Erythoxylun coca which is found throughout the Andes mountains. The use of cocaine dates back at least 5000 years among the Incas[3]. However in Europe, cocaine did not become popular until the 1860s when the active ingredient benzoy[1] methylecgonine hydrochloride, was isolated[4]. Prior to this time, the loss of potency during transport greatly suppressed the popularity of the coca plant.

In the past decade, the widespread use of cocaine has led to an increase in emergency department admissions for treatment of its acute toxic effects1. These effects include agitated delirium, seizure and stroke[2], myocardial ischemia and infarction[5,6], as well as tachyarrhythmias and myocarditis[7]. Episodes of silent myocardial ischemia have also been noted during the first weeks of cocaine withdrawal[8].

Although the relationship between cocaine toxicity and life-threatening cardiac events has been recognized historically as tempora[16], documentation of cocaine-induced coronary vasoconstriction has suggested this relationship to be causa[17]. Several mechanisms, however, have been proposed to explain cardiovascular complications subsequent to cocaine intoxication. These include, in addition to coronary artery spasm, focal coronary vasoconstriction[9], thrombus formation and platelet aggregation[10], direct myocardial toxicity[11], and increased myocardial oxygen demand[7].

ABOUT THE AUTHOR:

Dr. R. Gerace is a Professor in the Department of Medicine at The University of Western Ontario and Chairman of the Division of Emergency Medicine.

PHARMACOKINETICS

An understanding of the pharmacologic and toxicologic characteristics of cocaine is helpful in understanding clinical toxicity.

There are a variety of forms of cocaine that allow self administration. For example, cocaine hydrochloride, a white crystalline powder, is highly water soluble and administered intravenously or by nasal insufflation. Cocaine hydrochloride may be converted to the free-base form by dissolving the powder in an alkaline solution, using a solvent such as ether to extract the cocaine, and finally, evaporating the solvent. Crack is a form of free-base made using baking soda and water[4]. The free-base form of cocaine HCl vaporizes at temperatures greater than 98C without being destroyed, thereby allowing it to be smoked. Clinical effects associated with rapid absorption and ease of administration of free-base form was led to the popularity of smokable crack cocaine.

The pharmacokinetics of cocaine vary with the mode of administration of the drug. Cocaine is absorbed from various sites in the body including mucous membranes and the gastrointestinal tract. Following intranasal administration, the drug begins to exert its effects in about twenty minutes. The drug's half life may be several hours due to continued absorption. Smoking cocaine results in almost immediate pulmonary absorption and rapidly increasing blood concentration levels. Cocaine is rapidly and extensively metabolized by plasma and liver cholinesterases to the water soluble metabolites ecgonine methyl ester and benzoylecgonine[10].

PHARMACOLOGY

Once cocaine is absorbed, it produces its effects through local membrane stabilizing and sympathomimetic actions[10]. The primary target sites for the effects of cocaine include cardiovascular and neural tissues[12]. Initially, on the basis of central dopaminergic stimulation, cocaine produces euphoria and excitement, as well as an increase in heart rate and arterial blood pressure and in severe cases, arrhythmias and/or coma. This intense stimulation may be followed by anxiety, paranoia, and depression of respiration.

Cocaine has sympathomimetic as well as anaesthetic properties. By inhibiting sodium conductance, cocaine inhibits nerve impulse conduction. Cocaine also produces increased peripheral catecholamine levels by preventing presynaptic reuptake of neurotransmitters[12]. Cocaine's ability to directly stimulate central vasomotor centres compounds this drug's potential to create intense sympathetic stimulation. Small vessel vasoconstriction, increased vascular resistance, and increased cardiac output are among the drug's pathologic cardiovascular effects[13].

TOXICOLOGY

Although toxic effects of cocaine may be manifest in a variety of organ systems, including cardiovascular, neurologic, peripheral vascular, gastrointestinal, and musculoskeletal, the CNS and cardiovascular systems are responsible for most of the life-threatening complications seen. Specific neurologic complications include agitated delirium (intense paranoia)[14], cerebrovascular accident (potentially involving cerebral infarction, intracerebral hemorrhage, or subarachnoid hemorrhage)[15], and partial or generalized tonic-clonic seizures[16]. Seizures have been suggested as the single most lethal effect of cocaine toxicity[17]. Death in relation to cardiovascular complications, can result from ventricular fibrillation or asystole following doses as little as 20mg of parenterally administered cocaine. Recently, an increase in fatalities has been ascribed to cardiovascular and neurologic complications[1].

Blood levels of cocaine can be misleading. A 200-fold range of levels have been reported as lethal[11]. This is explainable given that susceptibility to the drug's toxic effects, as well as its metabolism, varies among individuals[18]. Therefore, cardiac and neurologic consequences, however, are not limited to large doses of cocaine[6].

CARDIOTOXIC EFFECTS OF COCAINE

Cocaine's cardiotoxic effects can result from all modes of administration of the drug6. Further, underlying heart disease is not a requisite for cocaine cardiotoxicity[19]. Stimulation of the central vasomotor centres and rising levels of peripheral catecholamines produce hypertension and tachycardia, as well as an initial increase in blood pressure. The drug's direct toxic effects on the myocardium may subsequently produce a fall in blood pressure. The sudden increase in myocardial oxygen demand, produced by an elevated heart rate and increased systemic arterial pressure, coupled with vasoconstriction of coronary blood vessels and resulting decreased oxygen supply, may override coronary autoregulation and produce the cardiovascular toxic effects associated with this drug[7].

Other potential theories that may explain the cardiotoxic mechanisms of cocaine in addition to acute myocardial infarction, coronary vasoconstriction, and arrhythmias, include platelet aggregation[10,19], contraction band necrosis[4,20], myocarditis[2,4], and cardiomyopathy (see figure 1)[10,21].

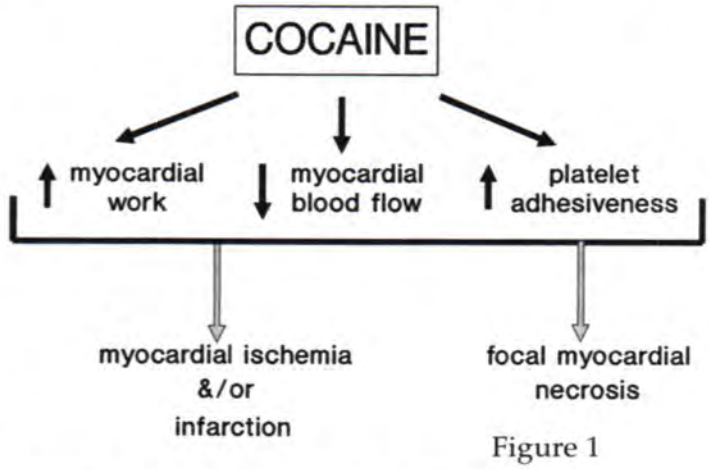


Figure 1

ACUTE MYOCARDIAL INFARCTION

The etiology of acute myocardial injury is multifactoria[1]. Cocaine's sympathomimetic effects elicit an increase in myocardial work. Coupled with a decrease in myocardial blood flow produced by coronary vasoconstriction and impaired pump activity, these toxic effects contribute to ischemia and perhaps, infarction. The combination of direct toxic effects of contraction bands and platelet adhesiveness, predispose to focal myocardial injury and, in the long-term, cardiomyopathy[21]. Furthermore cocaine may directly depress ventricular function in the absence of any acute myocardial injury. Acute ventricular dysfunction may occur as a result of sodium channel blockade.

Missing Pages

41-46

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. Degloving:
a) debridement of the palmar epidermal layer following burn injury;
b) intra-oral surgical exposure of the bony mandibular regions;
c) removal of procedure gloves following contamination of the surgical field;
d) post-operative anaesthesial phenomenon involving transient parasthesia of the upper limbs;

2. Xenophonia:
a) alteration in the quality of voice;
b) the adoption of a foreign voice due to schizophrenic delusions;
c) the quality of sound produced by a non-native speaker of a language;
d) the auditory hallucination of a non-self voice evident in schizophrenia;

3. Zonesthesia:
a) a loss of feeling or sensation involving multiple dermatomes;
b) area of focal numbness caused by local anaesthetic;
c) a zone characterized by swelling and loss of function caused by a zootoxin;
d) a sensation of constriction , as by a girdle;

4. Miliary:
a) a form of hyperkeratinized epithelial cyst;
b) pertaining to a cutaneous condition with retention of sweat;
c) characterized by lesions resembling millet seeds;
d) a erythemic sign;

5. Butyroid:
a) trademark for a preparation of butacaine sulfate;
b) an amino acid derivative of butyric acid;
c) an abnormal amount of saturated fatty acid residues in sweat due to chemical imbalance of the body;
d) resembling or having the consistency of butter;

6. Transfaunation:
a) genetic transformation in viruses;
b) genetic recombination of non-host DNA with host DNA;
c) transfer of animal parasites from one host to another;
d) Old English term for transformation;

7. Viraginity:
a) pseudohermaphrodism resulting in an inability to conceive;
b) a consequence of androgenization syndromes;
c) incapable of inducing ovulation;
d) a condition in which a woman has the sexual feelings and mentality of a man;

8. Perionyx:
a) a relic of the eponychium persisting as a band across the root of the nail during fetal development;
b) situated about the nailbed;
c) a kind of hypopyon;
d) an activating area associated with the dorsad region of the embryonic notochord;

9. Bubo:
a) a dome-shaped skin lesion with transient surface vesiculations;
b) inflamed lymph node, particularly in the groin or axilla;
c) the non-muscular component of the bulbococcygeus muscle;
d) a disease caused by consumption of the poisonous fruit of a tropical vine;

10. Fleckfeiber:
a) epidemic typhus;
b) intrinsic "trigger" to regulate diurnal rhythm;
c) a German department store;
d) a syndrome associated with a virulent pathogen of unknown origin;

11. Fragiform:
a) disruption of Haversian canal formation in bone;
b) shaped like a strawberry;
c) general description of any friable lesion;
d) none of the above;

12. Stomatomalacia:
a) any pathological condition of the mouth;
b) softening of tissue of the abdominal wall surrounding a colostomy/ileostomy opening;
c) a condition of body weakness;
d) abnormal softness of the oral structures;

13. Trichonodosis:
a) a fungal infection caused by species of Trichophyton;
b) the condition in which hairs are split and feather-like;
c) knotting of the hair as a result of inability of new hairs to grow from their follicles;
d) any disease or abnormal growth of the hair;

14. Meroacrania:
a) partly secreting;
b) a teratogenic consequence of organic mercury exposure;
c) partial congenital fissure of the cranium which extends into the cervical vertebrae;
d) congenital absence of part of the cranium;

15. Fourniere's Gangrene:
a) necrosis of a digit secondary to the use of epinephrine in a local anaesthetic preparation;
b) fulminating gangrene of the scrotum;
c) tracking of anaerobes fron a bite wound in the hand;
d) gradual onset psychosis secondary to sleep deprivation;

ANSWERS TO MEDICAL VOCABULARY

1. Degloving:
b) The exposure of the bony mandibular anterior or posterior regions by oral surgery.

2. Xenophonia:
a) Alteration of the accent and intonation of a person's speech.

3. Zonesthesia:
d) A painful sensation of constriction, as of a bandage bound too tightly, especially around the waist, also known as girdle sensation.

4. Miliary:
c) Characterized by lesions resembling millet seeds, as in miliary tuberculosis.

5. Butyroid:
d) Resembling or having the consistency of butter. Butyric acid is a four-carbon fatty acid found in rancid butter.

6. Transfaunation:
c) Transfer of animal parasites from one host to another.

7. Viraginity:
d) A condition in which a woman has the sexual feelings and mentality of a man.

8. Perionyx:
a) A relic of the eponychium persisting as a band across the root of the nail, seen in the eighth month of fetal life.

9. Bubo:
b) An enlarged and inflamed lymph node, particularly in the groin or axilla, due to an infection such as plague, syphillis, gonorrhoea, lymphogranuloma venereum, and tuberculosis.

10. Fleckfeiber:
a) Epidemic typhus.

11. Fragiform:
b) Shaped like a strawberry [L. fraga, strawberry].

12. Stomatomalacia:
d) Abnormal softening of the oral structures.

13. Trichonodosis:
c) A rare condition characterized by apparent or actual knotting of the hair thought to be the result of inability of new hairs to grow freely from their follicles because of abnormal toughness of the surrounding tissues.

14. Meroacrania:
d) A congenital absence of part of the cranium.

15. Fourniere's Gangrene:
b) Fulminating gangrene of the scrotum.

ANSWERS TO CASE STUDY

1. Was there any blood in the emesis or diarrhea? Not in his emesis; he did not look at the diarrhea. Did anyone else eat the mushrooms? His wife only had a teaspoonful full. (She was worried they were not safe.) She has had a small amount of diarrhes and has thrown up twice.
2. He has not kept anything down for 12 hours and is dehydrated. Start an IV and give him some normal saline. It would be kind to also give him some Gravol for the nausea. Because mushrooms can cause renal and hepatic failure you need to do some routine blood work including renal and liver function tests and a PT/PTT.
3. Who knows. You would expect him to be hypokalemic from all the diarrhea. Perhaps it was from damaged liver cells. He needs an EKG (look for peaked T waves) and gases done. He is at risk of going into v.fib unless his K promptly lowered by driving it back into cells (give dextrose and insulin, and bicarb) and by eliminating it (with an ion-exchange resin such as Kayexalate).
4. Very worried. There are several different groups of mushrooms. The clinical effects vary with the type of toxin ingested. Considering he got sick more than 6 hours after he ate the mushrooms, the severity of the vomiting and diarrhes and that his AST is already up, he probably ate *Amanita* sp. Poisoning with this type of mushroom has a mortality of 20-30%!

The following **misconceptions** in the treatment of mushroom poisoning should be avoided.
1) Poisoning may be an allergic reaction or food poisoning secondary to bacteria;
2) Poisoning may be secondary to pesticides sprayed on the mushroom or to edible mushrooms laced with drugs (like PCP);
3) All people ingesting mushrooms must become ill;
4) Symptoms presenting after six hours can't be due to Amanitas ingestion;
5) Discharge of patients without follow-up despite recovery from GI symptoms when these symptoms occurred six hours post-ingestion;
6) Assessing toxin identification and considering antidotes take precedence over theories of supportive care;

Ω

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 journal 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).

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.

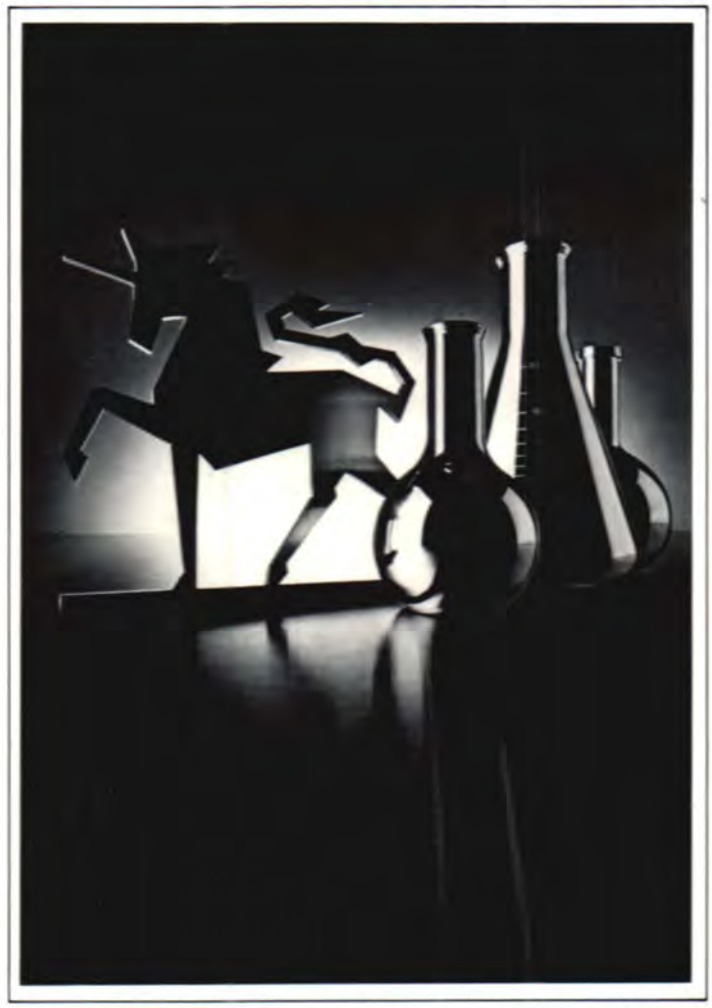
MODES OF COMMUNICATION: Authors should submit along with their manuscripts a cover letter including a return address, telephone number, and fax number (where available). The final revised version of the manuscript on 3.5" computer diskette should be sent (with (3) photocopies of the manuscript) to:

The Editors
U.W.O. Medical Journal
Health Sciences Building;
University of Western Ontario
London, Ontario N6A-5C1

Ω

THE POWER TO HEAL

The Wellcome Trust has donated well over one and one half million dollars to medical schools and libraries throughout Canada.



The Wellcome Foundation Ltd., of which we are one of the worldwide constituents, is a unique organization in the pharmaceutical industry.

Our symbol, the unicorn, is linked to the power to heal and cure. The advancement of medicine and the detection, prevention and cure of disease is our high goal, as it is yours.

WELLCOME MEDICAL DIVISION
BURROUGHS WELLCOME INC.
KIRKLAND, QUÉ.

PAAB
CCPP

W-8904