$10.00 per year

Publications Mail Registration No. 5363
Halifax, N.S.

THE NOVA SCOTIA MEDICAL JOURNAL

VOLUME 72 - NUMBER 1

The Journal is published bi-monthly by
The Medical Society of Nova Scotia
5 Spectacle Lake Drive
City of Lakes Business Park
Dartmouth, Nova Scotia
B3B 1X7
Phone (902) 468-1866
Fax: (902) 468-6578
and printed by
McCurdy Printing & Typesetting Limited

GUEST EDITORIAL

Cancer Treatment and Research Foundation of Nova Scotia

P.J. Fitzpatrick,* MB, BS, FRCPC, FRCR

An Act to Incorporate the Cancer Treatment and Research Foundation of Nova Scotia was enacted by the Governor and Assembly on June 5, 1980. Among its objectives were the establishment of facilities for the diagnosis and treatment of cancer, research, the education and training of health personnel and the maintenance of a central cancer registry.

The Halifax Clinic of the CTRFNS opened its doors on the ground floor of the Dickson Ambulatory Care Centre of the Victoria General Hospital on April 2, 1982 with the first patient being treated in September. It provides clinics for the assessment and follow-up of cancer patients organized through multidisciplinary tumour site groups. Comprehensive facilities for the non-surgical treatment of cancer by radiotherapy and chemotherapy are also provided. The name of the facility was changed to the Nova Scotia Cancer Centre on April 1, 1992 in order to better reflect its activities.

A provincial cancer registry was started in 1964, supported by a national health grant under cancer control programs. The act provided for the cancer registry to become the legalized responsibility of the CRTF. The legislation states that the objective of the cancer registry is to provide a central registry for the analysis and retrieval of data on cancer patients. The provision of an accurate and current cancer data base to meet the present and projected demands for information is listed in the Mission Statement of the CTRFNS. Health care in Nova Scotia costs 1.3 billion dollars a year and a significant proportion of this is devoted to cancer care. Without accurate information, particularly in relation to outcomes, it is impossible to know how appropriate are these expenditures. Today, approximately one in three persons will develop a malignancy at some time during their lives. In Nova Scotia, we expect to see approximately 4,000 new cases annually of whom one-half will die from their disease. Only heart disease is a greater cause of death. Cancer gets more common as we get older and as the population ages we can expect to see more cases of cancer and increased health care costs for cancer

* Physician-in-Chief, Cancer Treatment and Research Foundation of Nova Scotia, Halifax Clinic.

management. At present the cancer registry only records the incidence of various cancers and the county of residence at the time of diagnosis. It is planned to expand it in the future in order to be able to record mortality, survival, the various interventions used and measurements of outcome.

In order to document past practice and to help clearly define present policies for the management of different cancers it was decided to review the CTRF clinic records and compare them with data from the provincial tumour registry. To start the process we chose to review patients with breast cancer seen at the CTRFNS Halifax Clinic between 1980-1987. An ongoing audit of health records is required to determine the quality of both the care delivered and the data base necessary to measure treatment outcomes. The study reported elsewhere in this *Journal* found that there was inadequate information to make a comprehensive report on breast cancer in Nova Scotia. A similar position is likely to be encountered in other cancer centers and hospitals. It emphasizes the need for quality assurance programs to maintain the standards set for accreditation by the Canadian Health Management Council. We conclude that complete health records and accurate cancer registry data require the efforts of many professionals. There must be an adequate budget to finance a quality assurance program including the services of a full time epidemiologist and the necessary support staff. In particular, we emphasize the importance of physician commitment to maintain a readily retrievable, high calibre data resource for accurate outcome measurements. Information obtained from this study on breast cancer has provided the basis for the now documented necessary minimum information requirements that are essential for coordinated patient care and clinical research in cancer. □

Comment by Editor:

Recently, the Oncology Services Task Force of the Metropolitan Hospital Advisory Committee has issued its final report to the Metro Hospital Advisory Committee; it is now being discussed within the constituencies of the stakeholders. "A new vision" for the control of cancer and the care of patients living with cancer in Nova Scotia has been developed, and hopefully will be implemented within the next five years. The Metro Hospital Advisory Committee anticipates delivery of its final report to the Department of Health before the fall of 1993.

Correspondence

To the Editor:

GLOBAL POPULATION GROWTH

In the December 1992 issue you published an article by Dr. Michael McAlley of Chicago, Illinois in which Dr. McAlley makes an impassioned plea for North American physician's to take up the white man's burden and carry the gospel of population control to the developing world. Only a true believer in this gospel would make statements such as: "No goal is more crucial to the fate of the earth than stabilizing human population". This is surely a statement of faith. An equally ardent Christian could as earnestly say "No goal is more crucial to the fate of the earth than carrying the gospel of Christ to the whole world". Neither one of these statements is falsifiable and neither one belongs in a scientific journal.

Dr. McAlley prescribes population control as a panacea for all the world's problem: pollution, famine, urban poverty, refugees, maternal mortality, global warming, acid rain, loss of species, etc. All this, with only a passing reference to the likelihood that the earth's growing environmental problems are being caused by it's developed nations, not its developing ones. It seems that the Western world has learned how to control its population but has not learned how to control its greed for more and more of the world's resources.

Perhaps the real threat to the world's environment is teaching people that having VCRs and vacation homes is more important than having children. Perhaps the real threat to Hypocratic medicine is to view people as problems instead of patients.

Sincerely,

Philip Horner, MD, ABFP
150 Aberdeen Rd.
Bridgewater, N.S.
B4V 2S8 □

A Chart Audit: Reasons, Revelations, Recommendations

Günes N. Ege,* MD, FRCR, FRCPC, Peter J. Fitzpatrick,** MBBS, FRCR, FRCPC,
Thelma F. Croucher,† CCHRAC and Cindy Rogerson††

Halifax, N.S.

An ongoing audit of health records is required to determine the quality of both the care delivered and the data base necessary to measure treatment outcome. The objectives of a recent review of the charts of breast cancer patients seen at the CTRFNS Halifax Clinic between 1980-1987 were threefold:

a) to audit the process of identifying and retrieving charts of designated groups of patients;

b) to determine whether the current level of available clinical information constitutes an adequate data base; and

c) to review management and treatment outcomes.

This audit of 1175 charts has revealed inadequacies of the processes and the data base, both of which preclude any meaningful report regarding the outcome of the management of breast cancer in Nova Scotia. We conclude that complete health records and tumour registry data require the efforts of many professionals and emphasize the importance of physician commitment and involvement in maintaining a readily retrievable, high calibre data resource for accurate outcome measurements and for meeting the requirements of accreditation standards set by the Canadian Health Management Council.

Since its inception in 1982, the Cancer Treatment and Research Foundation of Nova Scotia (CTRFNS) has housed both the Cancer Registry (CR) and the Halifax Clinic. The Health Act of Nova Scotia requires that a report of any neoplasm diagnosed in a resident of Nova Scotia be forwarded to the CR whereby a CTRF number and chart are generated. Should the patient be referred to the Halifax Clinic for an opinion or further management, this record automatically becomes their clinic chart as well. Conversely, patients may be referred to the clinic immediately after diagnosis thus initiating their record in the CR. Not all cases recorded in the registry are referred to the Halifax Clinic. Since 1986 the CR has relied upon referring physicians to provide information on the patients' progress through the annual follow-up (FU) letter.

* Radiation Oncologist, CTRFNS, Halifax Clinic
** Physician-in-Chief, CTRFNS, Halifax Clinic
† Director, Health Record Department and Acting Director, Nova Scotia Cancer Registry
†† Fourth year student, Atlantic Veterinary College, Charlottetown, PEI.

Correspondence: Dr. P.J. Fitzpatrick, Cancer Treatment and Research Foundation of Nova Scotia, 5820 University Avenue, Halifax, N.S. B3H 1V7

The chart of a patient seen and followed up in clinic should constitute a complete record of the information required for an accurate diagnosis, results of investigations, interventions and management. Careful documentation of ongoing patient surveillance is designed to yield survival, morbidity, mortality statistics and determine prognostic factors. In 1983 a computerized patient information system was instituted for prospectively acquiring data to supplement records dating back to 1964.

Since the CR and clinic patient charts are the main repository for data on the incidence of cancer, patient management and survival in the province, it was appropriate to audit the quality of the data and the efficacy of retrieval for analysis and report.[1]

MATERIALS AND METHODS

Breast cancer was chosen for this audit since its prevalence would provide a large number of charts and a wide spectrum of issues for review. There were no figures available to distinguish referred patients with newly diagnosed breast cancer and those with recurrence who had had their initial treatment elsewhere. Since these groups could not be readily identified, a review of the charts of all patients with breast cancer seen between 1980-1987 was planned. The objectives were three fold:

a) to audit the process of identifying and retrieving charts of designated groups of patients and the ease and efficiency with which this could be achieved;

b) to determine whether the current level of clinical information available on patients with breast cancer would constitute an adequate data base for results that could be compared with those of other major oncology centres across Canada; and

c) to review management practices and treatment outcomes in this group of patients seen within the clinic.

The focus was on patients whose primary management had been influenced by their referral to the clinic, distinct from those only entered in the CR. The process of identifying study patients was encumbered by the integration of both Provincial Cancer Registry entrants and clinic patients into the same data base. "Registry only" patients were specifically excluded from our review. The computer print-out listed the following attributes: date of diagnosis, chart number, treatment – surgery, radiation, chemotherapy, histology, site, stage, last contact, status – alive or deceased.

Since charts of deceased patients are stored off site, the review was confined to the charts of patients alive and

seen in the clinic for the first time between January 1, 1980 and December 31, 1987 in order to assess chart quality, computer data accuracy and referral practices. For the years 1980 - 1982 only, the charts of deceased patients were also reviewed in order to evaluate treatment outcome and survival at five to ten years.

RESULTS

The initial computer search identified 987 charts of alive (1980-1987) and deceased (1980-1982) patients. Of these, 171 charts were rejected because they did not meet the review criteria. According to the first set of data, 208 patients with primary breast cancer had been seen in the clinic between 1980-1982. In view of the incidence of breast cancer in Nova Scotia (Table I, column 3) this seemed a very low referral rate (208/1062 x 100 = 19.5%). A second computer print-out based on the date of clinic admission revealed significant disparity and resulted in 170 patients being added to the study. Eighteen other patients were rejected because "clinic admission" was to another hospital and not specifically to the Halifax Clinic. Of a study population of 378 patients, the exclusion of 170 charts reflects a 45% shortfall in trying to identify in one step all patients eligible for this review.

After individual chart review we could determine the percentage of patients with primary breast cancer listed in the Provincial Cancer Registry who were referred to the Halifax Clinic within three months of diagnosis between 1980 - 1982 (Table I). There were 304 (28.6%) patients with primary breast cancer seen in clinic compared with the 208 (19.5%) patients identified on the initial computer printout. Figures are not available for 1983-1987, since charts of deceased patients for these years were not reviewed.

In reviewing the accuracy of the computers records other deficiencies were identified. Dates recorded on the computer were often at variance with the dates in the patients records. There was a 20% error in the computer entry for initial treatment when compared with the information extracted from the patient charts. The site of the primary lesion in the breast was coded as unspecified in 55% of cases although it could be determined in 75% of the charts reviewed. Both the computer records and patient charts were incomplete and lacked essential data. After reviewing all available clinical and pathological information, a clinical and pathological staging according to the UICC TNM criteria could be determined in only 25% of the initial charts examined. Similar deficiencies were revealed in the subsequently reviewed 170 charts. The current status of patients is obtained either from the last clinic note or from a follow-up letter from the family physician. In 50% of patients, the last contact information on the computer printout is either missing or out-dated when compared with the clinic chart. A date of death is obtained from weekly Vital Statistics Department death lists through a laborious manual process of matching names and other identifying information with the CTRF computerized patient records. No QA measures were in place during the study years and many records were found to be incomplete or contained inaccurate information. A significant number of patients were lost to follow-up and ambiguities in the FU letter resulted in erroneous information from the family physician.

The available chart based information was also reviewed and several deficiencies identified: prognostic factors such as family history was not available in 60%, pathology reports varied and did not always provide information on prognostic indicators, and in some charts there was inconsistency between the initial referral information and finalized reports. Finally, there were significant gaps in patient follow-up since notes were rarely received from surgeons who have assumed the ongoing care of patients treated at the clinic, although all referring physicians receive a copy of the note generated by each patient clinic visit.

TABLE I

Year	Annual Incidence Report	Updated Incidence Report	Patients seen at the Halifax Clinic			% Patients Registered with Primary Breast Cancer Seen at the Halifax Clinic
			Primary	Rec/Mets	FU/Other	
1980	317	326	120	13	3	37%
1981	315	350	84	12	6	24%
1982	376	386	100	26	14	26%
	TOTALS	1062	304			29% Overall

DISCUSSION

Several authors have recently reiterated the importance of an ongoing audit as a significant component of quality assurance.[2-6] Distinction is made between a traditional chart review and an audit, where practice is measured against defined criteria and it is implied that changes will be implemented as an outcome of the audit.[2] In order to keep the process moving and manageable, an audit should have an objective, boundaries, criteria and standards.[4] The delivery of health care, particularly in the field of oncology, involves the participation of many professionals leading to extensive documentation of clinical findings, results of investigations, treatments and continuing assessment. Computerization has made it possible to record salient aspects of patient data in a form easy to access and retrieve. Physicians play a critical role in this process. They are the majority generators and

consumers of this information. Review of parameters common to different patient groups and treatments undertaken is frequently required to assess end-results, morbidity and mortality.

Other professionals require rapid access to demographic data regarding the relevant patient population in order to anticipate work-load and plan resource allocation. Information must be accurate, complete, and up-to-date. This is possible only if there is commitment by the entire health care team to the maintenance of a high quality of computerized and hard copy records. The resources required must not be underestimated. Oncologists must have the time and manpower to ensure the collection of all relevant clinical information, and adequate resources and qualified staff must be in place to ensure timely data entry, updating and correction. Shortcomings can only be identified when the system is tested under the circumstances of a chart review as was demonstrated by our undertaking. This study reveals deficiencies in data acquisition and patient records that are all correctable. However, lack of accurate staging, consistent management and follow-up data preclude any meaningful report on referral practices, treatment policies, disease-free interval, and survival of breast cancer patients in Nova Scotia in the early 1980s.

The outcome of this audit has highlighted the value of the process by identifying current deficiencies. The following steps have been taken to address these concerns:

1. A review of the necessary minimum information required for oncologic patients in order to provide an accurate data base for future studies and outcome measurements.
2. A change in the face sheet of the clinic chart to include salient information on each new patient and checks to ensure accuracy and updating.
3. Separation of the records of clinic patients from CR patients.
4. Coding of conditions associated with neoplastic disease for research access.
5. The review of all data by trained health record technicians to avoid errors and omissions.
6. Revision of the "Follow-Up" letter completed by other physicians sharing in the care of clinic patients to avoid ambiguity and improve the quality of available clinical information.

It is important for all physicians to recognize the importance of and their responsibility for providing and accruing accurate and relevant clinical information in compiling a sound data base of oncologic practice in Nova Scotia. Although the CTRFNS is pivotal in the coordinated delivery of multidisciplinary cancer care and clinical research, long-standing manpower shortages at the Halifax Clinic have precluded the devotion of physician time to the systematic scrutiny of computerized patient data. These issues are now being addressed so the standards of treatment and end results can be compared with practices and outcomes in oncology across Canada. □

ACKNOWLEDGEMENT

We are grateful to Karen Starratt, Rosalee Walker, Jackie Smith and the staff of the Health Record Department for their dedicated assistance and to Ann Titus and Elizabeth Forsythe for preparation of the manuscript.

References

1. *Nova Scotia Cancer Registry* - CTRFNS 1982 - 1991. 5820 University Avenue, Halifax, Nova Scotia, B3H 1V7.
2. Shaw CD. Criterion based audit. *Br Med J* 1990; **300**: 649-651.
3. Heath DA. Random review of hospital patient records. *Br Med J* 1990; **300**: 651-652.
4. Williams JG, Kingham MJ, Morgan JM, Davies AB. Retrospective review of hospital patient records. *Br Med J* 1990; **300**: 991-993.
5. Lyons C, Gumpert R. Medical audit data: counting is not enough. *Br Med J* 1990; **300**: 1563-1566.
6. McConnachie RW. Organization of audit in North Derbyshire District Health Authority. *Br Med J* 1990; **300**: 1556-1558.

MOM — The Medical Office Manager

MOM is a fully accredited system written in close cooperation with practising physicians. **MOM** is extremely easy to use and is packed with features designed to simplify the operation of your practice. **MOM** handles the dull routine leaving you and your staff with time for more useful activities. No other system even approaches **MOM**'s level of capability. This, together with our unmatched support and low prices, is why people are abandoning other systems for **MOM**.

A Few of the Features MOM Offers

- *Complete MSI/WCB/Out of Province Claims Submission*
- *Private Billings to Patients, Companies, etc.*
- *Automatic Claim Reconciliation from MSI Floppy Disks*
- *Detailed Financial/Administrative Reporting*
- *Automatic Claim Validation*
- *Popup Calendar for Hospital Visit Claims*
- *Anaesthetic Claims Automatically Tagged with Start/End Times, Time Used & Units Breakdown*
- *Automatic Determination of Premium Fee Eligibility*
- *Automatic Capture of Patient Dx History*
- *Automatic Dx Look-up*
- *Idiosyncratic Dx Abbreviations*
- *Sex Specific Dx Checking*
- *Complete ICD9 File Included*
- *Automatic MSI Code Look-up*
- *Referral Physician Table with Automatic Look-up & Selection*
- *Referral Correspondence Management*
- *Automatic Letter Generator for Referral Correspondence*
- *Locates Patients by MSI Number, Name, Part of Name, What the Name "Sounds Like" or Hospital Unit Number*
- *Stores Patient Prescription Records, Test Results, Consultation Reports, Drug Allergies, Risk Groups, Hospital Unit Numbers, General Notes*
- *Generates Patient Addresses from Postcodes*
- *Inbuilt Canadian Classification of Diagnostic, Surgical & Therapeutic Procedures (CCDSTP)*
- *Automatic Capture of Procedures Performed with Ability to Refine Procedure Definition using CCDSTP*
- *Follow-up Notes & Success Rating for Procedures*
- *Drug Interaction Analysis*
- *Interface to Carefile™ Program*
- *Direct Access to Word Processor*
- *Comprehensive & Highly Selective Label Generation System for Address, Chart, Specimen Labels*
- *Personalized Form Letters*
- *Formal Analysis of Variance ("F" Test) on Patient Test Results*
- *Data Export for External Statistical Analysis*
- *Downloading Claims Data from Hospital Computers (Where Authorized by Hospital)*
- *Appointments System*
- *Reminders & Confirmations for Long-Term Appointments*
- *Individual Physician Waiting Lists*
- *External Clinic Appointments System*
- *Telephone/FAX/Pager List*
- *Automatic Forward Scheduling for Vaccinations & Other Procedures*
- *Pregnancy Lists*
- *Hospital Admission/Discharge Lists*
- *Patient Profile Files*
- *Patient History Reports for Insurance Companies etc.*
- *Surgery List*
- *Handles GST*
- *Multi-User Systems with Instant Windowing Available*

Plus

Low Prices

Prices start at **$449.99** for the "**MOM Jr–**" system which handles all types of claims for GPs and specialists (including anaesthetists) and comes with the full ICD9 file plus all MSI Claim Codes on board. **MOM Jr–** will handle ANY number of doctors.

Training

MOM customers can have as much training as they require. Since **MOM** is so easy to use you'll find you don't have to waste much time on training. Some of our users have never had any and don't think they need any — **MOM** is simple!

Support

MOM users receive unequalled support. For the first 12 months, telephone support is free as are site visits anywhere in the Province. We can offer this because our users have very few problems. Beyond 12 months a small annual fee provides continuing care.

CALL TODAY

If you want the best system for your practice call for a demonstration in your office at a time that suits you!

Benneworth Advanced Systems Inc.
59 Melwood Ave., Halifax
P.O. Box 5006
Armdale, NS B3L 4M6

Tel: 479-0300
Fax: 479-3099

BAS

Progress in Cancer Treatment Symptom Control

ALLEVIATION OF EMESIS BY THE 5-HT$_3$ RECEPTOR ANTAGONISTS

Stephen M. Sagar,* BSc, MBBS, MRCP, FRCR, FRCPC

Halifax, N.S.

BACKGROUND

Nausea and vomiting are side-effects of numerous chemotherapy treatments and certain radiotherapy techniques involving irradiation of the upper abdomen.[1]

Without reliable antiemetics, 100% of patients receiving high-dose Cisplatinum will vomit, and up to 75% of patients administered the adjuvant breast cancer regimen of CMF may suffer nausea and vomiting.[2] Unless directly questioned, many outpatients will not spontaneously inform the doctor of these symptoms and emesis has been ranked as the most distressing side-effect of chemotherapy.[3] Quality of life and ability to work may be severely compromised unless nausea and vomiting are adequately controlled.

Metoclopramide (Maxeran) at conventional doses and dimenhydrinate (Gravol) have not been demonstrated in controlled comparative studies to be more effective than placebo in treating chemotherapy- or radiotherapy-induced nausea or vomiting.[4,5,6] The recent improvement in antiemetic trial methods, with stratification for patient demography and chemotherapy regimens, has provided meaningful data on antiemetic efficacy. Dexamethasone has proven to be effective in reducing the symptom of nausea as well as vomiting, particularly when administered with other antiemetic agents such as prochlorperazine and domperidone.[7] The efficacy of the cannabinoids has been disappointing. Metoclopramide at very high dose is particularly effective in reducing cisplatinum-induced emesis but must be administered as an inpatient and has an unacceptable incidence of side-effects such as extra-pyramidal reactions (movement disorders) and sedation.[8]

THE 5-HT$_3$ RECEPTOR ANTAGONISTS

A recent medical breakthrough is the understanding of the mechanism for cancer treatment-related emesis. Cytotoxic drugs and radiotherapy directed to the upper abdomen induce the release of a transmitter termed Serotonin (5-HT) from enterochromaffin cells in the upper gastrointestinal tract. Serotonin interacts with the receptors on vagus nerve terminals which relay to the vomiting centre in the brain stem. Evidence from animal research, utilizing the ferret, demonstrated that specific antagonists of a serotonin receptor subtype (5HT$_3$) prevented vomiting.[9] Two 5-HT$_3$ receptor antagonists are now released for clinical use. The first is Ondansetron (Glaxo) which is currently available in Canada for either intravenous or oral administration. Granisetron (Smithkline Beechham) is not yet available in Canada but is licensed in the UK for intravenous administration only.

Extensive clinical evidence indicates that these are the most effective antiemetics available in preventing or curtailing vomiting or retching during the initial 24 hours following highly-emetogenic chemotherapy or irradiation of the upper abdomen (Fig. 1). Their efficacy *after* 48 hours and ability to significantly reduce *nausea* have still to be proven. However, there is no doubt that the addition of dexamethasone and its continuation during the following week markedly potentiates the antiemetic effect of the 5-HT$_3$ receptor antagonists, reduces nausea and increases appetite.[10,11] For *moderately* emetogenic chemotherapy, dexamethasone alone may be as effective as ondansetron, but the trial which addressed this issue was flawed by utilizing a suboptimal dose of ondansetron.[12]

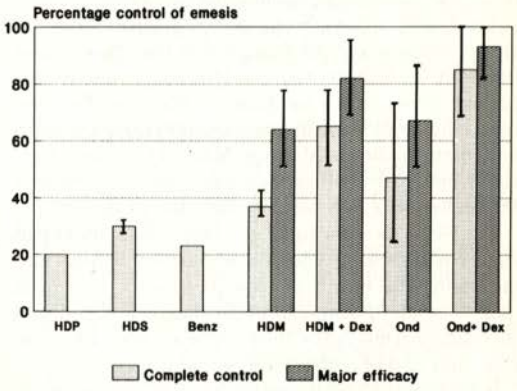


Fig. 1
Comparative survey of trials of antiemetic efficacy in cisplatin-induced emesis.

HDP = high dose prochlorperazine
HDS = high dose steroids
BENZ = benzodiazepines
HDM = high-dose metoclopramide
HDM+DEX = high-dose metoclopramide and dexamethasone
OND = ondansetron
OND+DEX = ondansetron + dexamethasone
Major efficacy = Two or less vomiting episodes (including any degree of nausea).

* Radiation Oncologist, Cancer Treatment and Research Foundation of Nova Scotia, Nova Scotia Cancer Centre, 5820 University Avenue, Halifax, N.S. B3H 1V7

Oral ondansetron almost completely controls vomiting secondary to irradiation of the upper abdomen, which may be included when treating bone metastases and abdominal lymph nodes.[13,14] As a consequence, inpatient admission for intravenous hydration is prevented and complications secondary to pathological fractures induced by retching are reduced. Ondansetron is being investigated as an antiemetic agent following abdominal surgery and general anaesthesia but is not currently licensed for this purpose (Glaxo: Personal communication). It is completely ineffective for motion sickness, labyrinthine disorders and emesis induced by morphine.

Despite variable pharmacokinetics, the degree and period of efficacy of ondansetron and granisetron are comparable and the side-effect of headache is similar.[1,15] Recent evidence suggests that an *oral* dose of 8 mg ondansetron repeated after 12 hours is as effective as 8 hourly administrations and as effective as either intravenous ondansetron or granisetron.[16,17]

COST-EFFICACY AND QUALITY OF LIFE

The hospital cost of 8 mg oral ondansetron is $17-40 and 10 mg IV ondansetron is $38-70 (Victoria General Hospital Pharmacy Information: Personal communication). Oral ondansetron utilized twice daily for no longer than 48 hours is likely to be the most cost-effective regimen and, during a 24 hour period, the cost is comparable to high dose i.v. metoclopramide and may avoid distressing side effects and hospital admission.

The CTRF of Nova Scotia currently underwrites the cost of ondansetron administered in the clinic but, in line with the Victoria General Hospital, is not able to finance prescriptions for patients after they have returned home. MSI and Pharmacare do not reimburse for ondansetron whereas Maritime Medical Care does. Currently, most patients must finance the cost of ondansetron themselves once they have left the clinic or hospital.

The 5-HT_3 receptor antagonists may reduce the cost of cancer treatment by allowing ambulatory therapy and facilitating the return of patients to work. Improved quality of life during cancer treatment and reduced psychological morbidity[17] may not be as expensive as the face value cost of ondansetron would suggest.

Future research addresses the issues of delayed vomiting , nausea, fractionated radiotherapy to the abdomen and comparative studies between ondansetron and granisetron. Cost-efficacy studies and quality of life issues will be relevant to the future use of the 5-HT_3 receptor antagonists.[18,19,20,21] □

ACKNOWLEDGEMENT

Mrs. Murdell Hall for typing this manuscript.

References

1. Sagar SM. The Current Role of Antiemetic Drugs in Oncology: A Recent Revolution in Patient Symptom Control. *Cancer Treatment Reviews* 1991; **18**:95-135.
2. Laszlo J and Lucas VS. Emesis As A Critical Problem in Chemotherapy. *New Engl J Med* 1981; **305**:948-949.
3. Coates A, Abraham S, Kaye SB, *et al.* On the receiving end: Patient perception of the side-effects of cancer chemotherapy. *European Cancer Clin Onco* 1983; **19**:203-208.
4. Cunningham D, Evans C, Gazet J-C, *et al.* Comparison of antiemetic efficacy of domperidone, metoclopramide and dexamethasone in patients receiving outpatient chemotherapy regimens. *Brit Med J* 1987; **295**:250.
5. Frytak S and Moertel CG. Management of nausea and vomiting in the cancer patient. *JAMA* 1981; **245**:393-396.
6. Stoll BA. Radiation Sickness: An analysis of over 1000 controlled drug trials. *Brit Med J* 1962; **1**:507-510.
7. Editorial. Corticosteroids and lorazepam as antiemetics in cancer chemotherapy. *Drugs Therapeut Bull* 1986; **24**:46-48.
8. Gralla RJ, Hin LM, Pisko SE, *et al.* Antiemetic efficacy of high-dose metoclopramide: randomized trials with placebo and prochlorperazine in patients with chemotherapy-induced nausea and vomiting. *New Engl J Med* 1981; **305**:905-909.
9. Bermudez J, Boyle EA, Miner WD and Sanger GJ. The antiemetic potential of the 5-HT_3 receptor antagonist BRL43694. *Brit J Canc* 1988; **58**:644-650.
10. Smith DB, Newlands ES, Rustin EJS, *et al.* Comparison of ondansetron and ondansetron plus dexamethasone as antiemetic prophylaxis during cisplatin-containing chemotherapy. *Lancet* 1991; **338**:487-490.
11. Smyth JF, Coleman RE, Nicolson M, *et al.* Does dexamethasone enhance control of acute cisplatin induced emesis by ondansetron? *Brit Med J* 1991; **303**:1423-6.
12. Jones AL, Hill AS, Soukop M, *et al.* Comparison of dexamethasone and ondansetron in the prophylaxis of emesis induced by moderately emetogenic chemotherapy. *Lancet* 1991; **338**:483-487.
13. Priestman TJ, Roberts JT, Lucraft H, *et al.* Results of a randomized double-blind study of ondansetron and metoclopramide in the prevention of nausea and vomiting following high dose upper abdominal irradiation. *Clin Oncol* 1990; **2**:71-75.
14. Roberts JT. Ondansetron in the control of refractory emesis following radiotherapy. *Clin Oncol* 1992; **4**:67-68.
15. Logue JP, Magee B, Hunter RD and Murdoch RD. The antiemetic effect of granisetron in lower hemibody radiotherapy. *Clin Oncol* 1991; **3**:247-249.
16. Seynaeve C, Schuller J, Brunner KW, *et al.* Comparison of the antiemetic efficacy of different doses of ondansetron given as either a continuous infusion or a single intravenous dose in acute cisplatin-induced emesis. *Brit J Canc* 1992; **66**:192-197.
17. Watson M, McCarron J and Law M. Anticipatory nausea and emesis, and psychological morbidity; assessment of prevalence amongst out-patients on mild to moderate chemotherapy regimens. *Brit J Canc* 1992; **66**:862-866.
18. Sands R, Roberts JT, Marsh M and Gill A. Low dose ondansetron and dexamethasone: A cost-effective alternative to high-dose metoclopramide/dexamethasone/lorazepam in the prevention of acute cisplatin-induced emesis. *Clin Oncol* 1992; **4**:67.
19. Soukop M. Emesis control and quality of life during repeated chemotherapy for breast cancer. Ondansetron Satellite Symposium: The Sixth European Conference on Clinical Oncology and Cancer Nursing (ECCO-6) Florence, Italy, October 1991: 34-40.
20. Cunningham D, Gore M, Davidson N, Miocevich M, Manchanda M and Wells, N. The real costs of emesis – An economic analysis of Ondomsetron vs Metoclopramide in controlling emesis in patients receiving chemotherapy for cancer. *Eur J Cancer* 1993; **29A**:303-306.
21. Buxton MJ and OBrien BJ. Economic evaluation of ondansetron: a preliminary analysis using clinical trial data prior to price setting. *Br J Cancer* (1992); **66** (suppl XIX):64-67.

"There are only two sorts of doctors:
those who practise with their brains,
and those who practise with their tongues."

Sir William Osler (1849-1919)

Gestational Trophoblastic Disease Registry

UPDATE 1990

John Jeffrey,* MD, FRCS(C), I. Zayid,** MD, FRCP(C), M.L. Givner,† PhD and M. Trott,†† RN

Halifax, N.S.

A total of 27 new patients were entered into the Nova Scotia Gestational Trophoblastic Disease Registry and Surveillance Program in 1990. Two patients were confirmed to have benign hydatidiform mole (HCG titres return to normal with no treatment other than the original D&C); two patients developed MGTD; one patient was diagnosed with a choriocarcinoma: twenty-two patients had partial (incomplete) mole; (Tables I and II).

TABLE I

1. **Benign GTN**
   A. Hydatidiform Mole
2. **Malignant GTN**
   A. Non-metastatic (NMGTD)
      1. Persistent Hydatidiform Mole
      2. Invasive mole
      3. Choriocarcinoma

   B. Metastatic GTN (MGTD)
      1. Good prognosis, low risk
      2. Poor prognosis, high risk
         a) Initial urinary HCG titre > 100,000 IU/24 hr. or serum HCG title > 40,000 m1U/ml
         b) Duration of symptoms > 4 months
         c) Liver or brain metastasis
         d) Previous chemotherapy
         e) Disease following term pregnancy

TABLE II

EXPERIENCE OF THE TROPHOBLASTIC DISEASE REGISTRY IN 1990

1.	**Benign GTD**	
	A. Hydatidiform mole	2
2.	**Malignant GTD**	
	A. Nonmetastatic (NMGTD)	
	1. Persistent hydatidiform mole	0
	2. Invasive mole	0
	3. Choriocarcinoma	1
	B. Metastatic GTD (MGTD)	2
	Partial mole	22
	Placental Site Trophoblastic Tumor	0
	TOTAL	**27**

From the Nova Scotia Gestational Trophoblastic Disease Registry, Department of Obstetrics and Gynaecology, Dalhousie University, Halifax, N.S.
*Director, Gynaecology Oncology, Victoria General Hospital
**Director Anatomical Pathology, Department of Pathology, D.J. MacKenzie Diagnostic Center
†Head, Endocrinology Lab, Victoria General Hospital, and Associate Professor of Pathology, Dalhousie University
††Co-ordinator GTD Registry

GLOSSARY:

HCG – Human Chorionic Gonadotrophin (Amerlex-M serum Beta sub unit assay)

NMGTD – Non-metastatic gestational trophoblastic disease

MGTD – Metastatic gestational trophoblastic disease

PRESENTATION

Abnormal vaginal bleeding remains the commonest presentation for the hydatidiform mole. Ultrasound as well, plays a major part in the diagnosis. Of the 5 patients referred to the registry (including benign and non-metastatic disease) all 5 patients had ultrasound determinations performed. Three ultrasounds were positive for hydatidiform mole. Of the two patients who had negative ultrasound examinations, one patient was subsequently found to have a molar pregnancy following at D&C for a missed abortion; the second patient was diagnosed with choriocarcinoma following a hysterectomy for persistent refractory bleeding. In this small group of patients, this represents a false negative rate of 40% for ultrasonography.

BENIGN HYDATIDIFORM MOLE

Of the 2 patients confirmed to have hydatidiform mole, one patient had titres return to normal in 10 weeks and the other in twelve weeks.

One patient was referred to the registry by her gynaecologist, the other by the pathology department.

The mean age of these 2 patients was 23.5 years. One patient presented with the symptom of abnormal vaginal bleeding and the other patient exhibited excessive nausea and vomiting. The patient with the abnormal vaginal bleeding had ovarian enlargement as well. Both patients were noted to have a uterus large for their dates.

Malignant Gestational Trophoblastic Disease

A. Nonmetastatic (NMGTD)

1) *Persistant hydatidiform mole*
No registered cases in 1990.

2) *Invasive mole*
No cases of invasive mole registered in 1990.

3) *Choriocarcinoma*
One case of choriocarcinoma was registered in the

1990 year. This patient had a caesarian section performed for term delivery of the baby. Following two D&Cs and a hysterectomy for persistent bleeding, a diagnosis of choriocarcinoma was made. Metastatic work up was negative. The patient was treated with 3 courses of a combination of VP16, Actinomycin-D and Methotrexate with Leucovorin rescue. Titres were normal after 2 courses of chemotherapy and follow up has been uneventful to date.

B. Metastatic gestational trophoblastic disease

Two patients were registered with metastatic gestational trophoblastic disease.

The first patient, 20 years of age, was referred for a therapeutic abortion. At presentation, the patient was noted to have had some vaginal bleeding and a uterus large for her dates. An ultrasound was performed and was in keeping with a hydatidiform molar pregnancy. The pre D&C Beta sub unit HCG titre was 158,889. Following D&C, titres initially fell to 1904 and then gradually climbed to 2503. Chest x-ray was positive for metastatic deposits on the right lung. Diagnosis was confirmed by tomograms. The remainder of the metastatic work up was negative. The patient received 7 courses of sequential chemotherapy involving alternating cycles of Actinomycin D and Methotrexate with Leucovorin rescue. HCG titres had returned to normal (three consecutive negative titres), 9 weeks after chemotherapy treatment was initiated. Chest x-ray was negative at 9 weeks as well. Contrary to registry recommendations, patient is presently pregnant with an ultrasound confirmed normal pregnancy.

The second patient, 33 years old, had a D&C for abnormal bleeding with her first pregnancy. D&C tissue report showed immature chorionic villi. A repeat D&C was done 4 weeks later for continued bleeding. Tissue report indicated a complete hydatidiform mole but with unusual presentation due to the presence of fetal parts. Beta sub unit HCG titre at the time of the second D&C was 10,239. Routine chest x-ray showed a lung lesion, which was confirmed with tomograms. Remainder of the metastatic work up was negative though a CAT scan of the pelvis showed a uterus increased in size. Patient was treated with sequential alternating courses of Actinomycin-D and Methotrexate with Leucovorin rescue every 2 weeks. HCG titre at the start of the treatment was 57,571. During treatment the patient, experienced severe abdominal pain controlled with anti-inflammatory agents and pain medication. A vaginal ultrasound showed an intramyometrial nodule in the uterine fundus which was felt to represent trophoblastic disease. Beta sub unit HCG titres returned to normal 2 months after the start of chemotherapy. Drug regimen was tolerated poorly. Follow up has been uneventful to date at the 7 month mark. The intramyometrial nodule has completely regressed.

TOTAL EXPERIENCE – GESTATIONAL TROPHOBLASTIC DISEASE REGISTRY

A total of 462 patients (partial mole excluded) have been registered by the Nova Scotia Gestational Trophoblastic Disease Registry as of December, 1990. (Table III)

TABLE III

NOVA SCOTIA GESTATIONAL TROPHOBLASTIC DISEASE REGISTRY

TOTAL EXPERIENCE (Excludes Partial Mole)

	1965-75	1976-80	1981-85	1986	1987	1988	1989	1990
Nova Scotia	40(12)	108(13)	72(14)	18(1)	12(1)	11(2)	9(3)	3(2)
New Brunswick	8 (6)	31 (2)	46 (8)	5(3)	3	8(2)	6(2)	1(1)
Prince Edward Island		4 (0)	9 (0)	0	2	2	2	1(0)
Newfoundland		15 (4)	39 (5)	0	2	2	1	0
St. Pierre		1 (0)						0

Total number of patients – 462

Total requiring Rx 78 or 16.8% (in parenthesis)

Benign Gestational Trophoblastic Disease

Hydatidiform Mole

Three hundred and seventy-nine patients were confirmed to have benign hydatidiform mole requiring no treatment other than the original D&C. (Table IV)

TABLE IV

NOVA SCOTIA GESTATIONAL TROPHOBLASTIC DISEASE REGISTRY

1. Benign GTD		
A. Hydatidiform mole		379
2. Malignant GTD		
A. Nonmetastatic (NMGTD)		
1. Persistent hydatidiform mole		58
2. Invasive Mole		0
3. Choriocarcinoma		4
B. Metastatic GTD (MGTD)		19
Non gestational choriocarcinoma		1
Placental site trophoblastic tumor		1
	TOTAL	462

Malignant Gestational Trophoblastic Disease

Nonmetastatic (NMGTD)

Fifty-eight patients developed persistent nonmetastatic gestational trophoblastic disease. Four of these patients developed histologically confirmed choriocarcinoma. (Table V) All 58 patients remain alive and well.

TABLE V

CHORIOCARCINOMA (confirmed histologically)

	Metastatic	Nonmetastatic
Post Ectopic	1	
Post molar pregnancy		1
Post normal pregnancy	4 (3 died)	2
Etiology unknown *	1 (died)	
Post hysterectomy – DUB**		1

* recurrent choriocarcinoma – expired 1987
** positive pregnancy test

Six patients remain alive and well.

Metastatic Gestational Trophoblastic Disease

Nineteen patients developed persistent metastatic disease. Six of these had histologically confirmed choriocarcinoma. (Table V) Four of the patients with metastatic choriocarcinoma died. Three were diagnosed following a normal pregnancy and died either of advanced disease or complications of chemotherapy. The fourth patient, who presented with choriocarcinoma etiology unknown, had a 2½ year remission between the time of her original treatment and recurrence. She was treated extensively with chemotherapy but expired in 1987.

The remaining 15 patients with MGTD remain alive and well.

Non-gestational choriocarcinoma

One patient presented with non-gestational choriocarcinoma. This patient's case history was published in the 1987 registry report. Her HCG titres are now done once every six months and remain normal.

Placental Site Trophoblastic Tumor

This patient's case history was presented in the 1989 report and she continues to do well at the 12 month mark in follow up.

THE INCOMPLETE OR PARTIAL MOLE

In 1981 a study to evaluate the clinical significance of the partial mole (hydatidiform degeneration) was begun.

To date 92 patients, with partial mole have been followed by the registry. Dr. I. Zayid of the Dr. D. J. MacKenzie Diagnostic Centre has reviewed the pathology on 90 of these patients. Two patients were lost to follow up.

Of these patients, 68 had HCG titres which returned to normal in ten weeks or less; 11 patients had titres which took 10-14 weeks before returning to normal, 10 patients entered the study late (8 at 11 weeks, 1 at 18 and 22 weeks) and their titres were normal at entry. One patient was non-compliant with HCG follow up.

Follow up for the 92 patients has been uneventful and ranged from five to twelve months (eighty-two patients) one to two months (seven patients).

In 1990, 22 patients were diagnosed with partial (incomplete) mole.

Nineteen of these patients had titres return to normal in 4-10 weeks and six patients had titres which took 10 to 12 weeks before returning to normal.

These 22 patients had a median age of 28 years with one age not recorded. Eight patients were referred to the registry by pathologists, 11 referred by gynaecologists, 2 patients were referred by family physicians and 1 patient was picked up on review of titres by the registry coordinator.

Twenty of the 22 patients followed in 1990, experienced vaginal bleeding, 8 complained of abdominal pain and 1 patient presented with excessive nausea and vomiting. One patient presented with shortness of breath, 1 with fatigue and 1 patient had no symptoms. The size of the uterus was smaller than dates in 11 patients. Larger than dates in two patients. Uterine size was appropriate for dates in 2 patients and there was no record on 7 patients. Fourteen of the 22 patients had ultrasound examinations performed. Eleven of the 14 ultrasounds were not diagnosed as a mole.

The registry will continue to recommend 6 months of follow up with HCG titres for the patient with partial mole. This decision is based on information which suggests that 5-9% of patients with partial mole will develop persistent gestational trophoblastic disease. (World Congress on Trophoblastic Disease, 1990)

FOLLOW-UP RECOMMENDATIONS

Between 15-20% of the patients who have had a molar pregnancy will require adjunctive chemotherapy or an occasional patient will require surgery to eradicate their disease. For this reason follow-up with HCG titres is essential. Registration with the Trophoblastic Disease Registry is recommended for all cases and can be made by writing to:

N.S. Gestational Trophoblastic Disease Registry
Room 5054, Ambulatory Care Center
Victoria General Hospital
Halifax, N.S. B3H 2Y9
by phoning (902) 428-2263
or by FAX (902) 428-3765

The follow up protocol for patients with gestational trophoblastic disease as recommended by the Nova Scotia Gestational Trophoblastic Disease Registry is as follows:

After hospital discharge

a) HCG weekly until three consecutive normal values are achieved. Then . . .
b) HCG monthly for one year. Pregnancy is permissable after 6 months of normal titres. If pregnancy is suspected an ultrasound is indicated for early confirmation.

Continued on page 24.

Routine Swan-Ganz Catheterization in Aortic Surgery

IS IT REALLY NECESSARY?

R.S. Dunn,* MD, FRCS(C), FACS, M.A. Naqvi,** MD, FRCS(C), FACS and Cameron Dunn†

Sydney, N.S.

During the past decade it has become standard practice in many hospitals throughout North America to include, as part of the pre-operative preparation of a patient undergoing aortic surgery, the placement of a right heart thermodilution catheter. The anesthetist then monitors wedge pressures, right heart pressures, and cardiac output determinations throughout the course of surgery and into the post-operative period. The literature contains many references to this procedure as being the gold standard for intra-operative monitoring of patients undergoing aortic aneurysm resection or aortic bypass surgery. It is well recognized that clamping and declamping of the aorta are associated with profound changes in myocardial and renal function, and the belief is widespread that these kinds of changes are dealt with more accurately using the information provided by indwelling pulmonary artery cathethers.

Despite the fact that these catheters have been in widespread usage for several decades, a recent review of all of the papers produced on the subject since 1962, has revealed that there is as yet no randomized prospective trial which has ever documented an improved outcome in patients monitored this way.[2]

In our institution we do use Swan-Ganz catheterization for a variety of critically ill patients, and in a variety of settings. However, it has never been standard practice to routinely insert this kind of pulmonary artery catheter preoperatively. Therefore, we have accumulated a significant number of patients that have been monitored intra-operatively without these invasive lines, and we felt it would be very useful to compare objective measures of outcome with generally accepted standards, to determine whether or not there were measureable differences.

The study was also given impetus because of recent severe fiscal restrictions which have affected O.R. time and hospital equipment, and O.R. budgets in Nova Scotia. Pre-operative preparation of the patient to include Swan-Ganz catheter, generally adds about an hour to the operative time for these patients and makes intra-operative monitoring and post-operative monitoring technically somewhat more complex. In addition, there is a direct impact on the hospital budget for hardware, and on the physician payment agencies in terms of fees for the service.

* General and Vascular Surgeon, Sydney City Hospital, Sydney, N.S.
** Vascular Surgery, Sydney City Hospital
† Clinical Research Assistant, Sydney City Hospital.

Correspondence: Dr. R.S. Dunn, 146 Whitney Ave., Sydney, N.S. B1P 1Z9

MATERIALS AND METHOD

The survey is a retrospective review of consecutive hospital charts in Sydney City Hospital for patients admitted for surgery with a diagnosis of abdominal aortic aneurysm or aorto-iliac occlusive disease. The years encompass 1981 to the end of 1990 (inclusive) – a 10 year period. The patients were divided into four groups: elective abdominal aortic aneurysm, or emergency abdominal aortic aneurysm; elective aorto-iliac occlusive disease, or emergency aorto-iliac occlusive disease. The usual demographic data were collected and included an analysis of risk factors, age, antibiotic prophylaxis, exact procedure performed, type of prothesis used, type of invasive monitoring used, post-operative complications and the reason the Swan-Ganz line may have been felt to be necessary in the post-operative period. We then collected any objective measures of outcome which seemed relevant to clinical practice, including: mortality rates, cause of death, hospital stay, days spent in I.C.U., days requiring mechanical ventilation, length of time in O.R., and intra-operative transfusions.

Indications for the use of the Swan-Ganz catheter in the post-operative period were very specific:

1. Persistent hypotension after adequate fluid resuscitation.
2. Persistent oliguria.
3. Evidence of congestive heart failure refractory to standard medical management.

RESULTS

Four hundred and twenty-three patients were collected in this series (Table I). A total of 197 aneurysms were operated, and 226 bypasses for aorto-iliac occlusive disease. Demographic data are presented in Table II. Risk factors identified are listed in Table III. Table IV indicates the usage of Swan-Ganz catheters over this 10 year period in our aortic patients. In only one, was a catheter inserted pre-operatively. A total of 24 patients were monitored at some point for an overall percentage of only 5.6%.

TableV indicates the days in I.C.U. post-operatively for this group of patients. For the majority, it was less than 3 days, and a significant proportion did not require intensive care treatment. It is not surprising that the group with the most prolonged I.C.U. stay were emergency aneurysms, most of those frankly ruptured aneurysms. The requirement for post-operative ventilation is illustrated in Table VI, with the majority being extubated on

the first day in all groups. Only a small proportion required prolonged ventilation and, once again, the emergency aneurysms fell into this category. Operative time, (Table VII), is the total anesthetic time, recorded the minute the patient enters the O.R. suite until they exit the O.R. suite. A significant proportion was in and out of the O.R. in less than 2 hours, and a larger proportion out of the O.R. in less than three. Long cases were dominated by the emergency aneurysm group.

TABLE I

THE STUDY GROUP

Year	AI	AI^E	AAA	AAA^E
81	29	1	12	3
82	19	1	13	6
83	24	2	15	6
84	19	3	7	3
85	17	6	5	5
86	16	1	25	6
87	30	1	14	10
88	17		17	3
89	20		20	3
90	20		18	6
TOTALS	211	15	146	51

GRAND TOTAL – 423

AI – Aorto-iliac occlusive disease
AI^E – Aorto-iliac occlusive disease, emergency
AAA – Abdominal aortic aneurysm
AAA^E – Abdominal aortic aneurysm, emergency

TABLE II

AGE AND MALE/FEMALE RATIOS

	AI	AI^E	AAA	AAA^E
Male/female ratio	2.1:1	2.6:1	4.1:1	4.8:1
Mean age (yr)	60.1	64.0	71.1	71.8
Age range (yr)	33-88	45-75	49-88	57-91

TABLE III

RISK FACTORS

Risk Factors	AI	AI^E	AAA	AAA^E
* Hypertension	34	2	30	6
* Smoker 1pk/day	115	12	87	26
Diabetes	37	1	6	4
Previous stroke	6	2	5	2
Previous MI	16	6	20	7

* Not always accurately recorded on charts – true numbers probably higher.

Post-operative stay in hospital for all groups combined is illustrated in Table VIII. The vast majority were out of hospital in less than 14 days, and a small number was able to be discharged in less than 6 days. The relatively small proportion (9.5%) of long-stay patients was dominated by the emergency group of patients, mostly abdominal aortic aneurysms.

TABLE IV

SWAN-GANZ CATHETERS UTILIZED

	PRE-OP	POST-OP	%
AAA		6	4
AAA^E	1	10	20
AI		6	2.8
AI^E		1	6.6
TOTAL	1	23	5.6

TABLE V

DAYS IN I.C.U.

	<1	1-3	3-5	5-10	>10
AAA	19*(13)	74(51)	33(23)	17(12)	3(2)
AAA^E	5(10)	22(43)	9(18)	8(16)	7(14)
AI	28(13)	130(62)	32(15)	17(8)	4(2)
AI^E	4(27)	4(27)	3(20)	3(20)	1(6)

* Values in parentheses are percentages

TABLE VI

DAYS POST-OP VENTILATION

	1 DAY	1-3 DAYS	3-5 DAYS	5 DAYS
AAA	104(71)*	34(23)	3(2)	4(3)
AAA^E	17(33)	20(39)	4(8)	10(19)
AI	155(73)	30(14)	4(2)	2(1)
AI^E	8(33)	5(33)	– –	2(13)

* Percentages are in parentheses

TABLE VII

TOTAL OPERATING TIME

	2 hr	2-3 hr	3-4 hr	4 hr
AAA	16(11)*	80(55)	34(23)	16(11)
AAA^E	8(15)	17(34)	13(25)	13(26)
AI	11(5)	127(60)	58(28)	15(7)
AI^E	2(12)	5(29)	4(28)	6(31)

* Calculated from the time the patient enters O.R. suite until the patient exits.

** Percentages are in parentheses.

TABLE VIII

POST-OPERATIVE STAY, ALL GROUPS COMBINED

	Days					
	6	7-10	11-14	15-18	19-22	22
No. patients	27	160	128	35	33	40
Percent	6.1	37.6	30.1	8.1	7.8	9.5

Major complications are listed in Table IX. Seriously ill patients often had more than one major complication.

TABLE IX

MAJOR COMPLICATIONS

Complications	AI	AI^E	AAA	AAA^E
* Renal failure (Dialysis)	1		1	
* MI	2	1	4	3
* Graft thrombosis or distal embolus	5	1	2	4
* Stroke	1			
* Infarcted bowel			1	6
* GI bleed	3	2	3	4
* Pulmonary embolus	2	1	2	
* Superficial wound infection	3			1
* Infected graft		1		
TOTALS	17	5	14	25

* Required further surgery

Intra-operative requirement for blood is illustrated in Table X. AI + AI^E were combined due to small numbers in the AI^E group.

Some patients undergoing aortic bypass for occlusive disease required no intra-operative transfusions. The majority received 2 units or less. Aortic aneurysms on average required more blood, although some could still be repaired without transfusion. It is in the emergency aneurysm group where transfusion requirements are much greater, and are naturally associated with greater degrees of shock and the ensuing intra-operative and post-operative difficulties.

Table XI presents raw data and percentages for mortality rates over the 10 year period in the four major categories.

TABLE X

INTRA-OPERATIVE TRANSFUSIONS

	*1-2 U	3-4 U	5-6 U	6 U
AAA	16(11)**	43(29)	60(41)	7(5)
AAA^E	4(8)	5(10)	9(18)	10(20) 22(43)
AI	70(33)	105(50)	30(14)	4(2) 2(1)
AI^E	2(13)	4(26)	5(33)	3(20) 1(6)

* Units packed cells

** Values in parentheses are percentages

TABLE XI

MORTALITY

Category	Number	Percent
AAA	6	4.1
AAA^E	21	38.8
AI	4	1.9
AI^E	2	6.7

DISCUSSION

A large number of publications document the benefits of monitoring critically ill patients with Swan-Ganz thermodilution catheters.[2] This technique allows ongoing determinations of right and left heart filling pressures and cardiac outputs, thereby allowing early diagnosis of left heart failure or overload, or even myocardial infarction. Fine tuning of fluid management intra-operatively and post-operatively is felt to be more accurate, especially in patients with poor left ventricular function.

With the widespread use of these catheters, a variety of disadvantages has also been reported. Firstly, there are well recognized complications in morbidity due to the insertion of these catheters. A partial list would include: hemorrhage, pneumothorax, air embolism, ventricular tachycardia, cardiac perforation, sepsis (2%), pulmonary artery rupture, and infusion of fluid into the wrong body space. Some of these complications are fatal. Secondly, inappropriate treatment due to incorrect readings are a constant problem in all intensive care units. There are many factors that must be satisfied in order to insure that the readings obtained as wedge pressures and cardiac outputs are, in fact, accurate. Some causes of incorrect readings include: re-warming of the injectate, incorrect volume of the injectate, bad tip position, high intrathoracic pressure, high peripheral vascular resistance, air bubbles in the lines, and other technical problems, and changes with respiratory cycle.

The financial impact of the routine implantation of these catheters pre-operatively is significant. The catheter prices vary widely, from $50 to $90 (Nova Scotia, 1990). But, when the transducers, tubing, and other hardware are included, the per case hardware cost is usually around $200.00. The physician fee in Nova Scotia for implantation is $132.00. In Nova Scotia in 1990, records indicate that 321 aortic procedures were carried out with a projected cost for invasive monitoring of $101,757.00. By comparison, the surgical fees for the same procedures would be less than twice the amount of $199,052.00. Not measured is the impact of the extra time in the O.R. list.

In our hospitals, the extra time taken for patient preparation comes off the surgeon's block time. Some 300 hours of surgical time then, were devoted to Swan-Ganz insertions in 1990.

We believe that our patient population of aortic aneurysms and aorto-iliac occlusions is similar to that in other centres across this Country. Efforts to scientifically stratify our patients with respect to cardiac risk, using one of the standard grading systems, would have been useful in this study. However, the nature of this retrospective review and the time available, did not allow such classification to be achieved with any degree of confidence. Nonetheless, we do believe that in a group of aortic patients as large as this, cardiac risk factors distribution would be very similar to that in a similar size group of patients from any institution practicing this type of surgery. The risk factors, and age structures, are all typical. We would submit that the post-operative requirements of our patients for

I.C.U. stay, mechanical ventilation, and post-operative hospital stay, are generally comparable to any major centre. Even though only 5.6 percent of these patients were monitored post-operatively with Swan-Ganz catheters for a variety of reasons, the ultimate measure of outcome, namely mortality rates, would appear to us to compare quite favorably with historically acceptable rates.[7,8]

A review of the literature indicates that a variety of authors throughout North America are questioning the necessity for routine placement of these indwelling catheters pre-operatively, not only in aortic surgery but also in coronary artery bypasses. Truman, *et al.* looked at 1,094 prospective coronary artery bypass graft patients and found no outcome difference in low-risk patients randomized to pre-op Swan-Ganz and no pre-op Swan-Ganz.[6] Bashein *et al* looked at 698 coronary artery bypass graft patients who did not receive Swan-Ganz catheters, and found a 1.5 percent mortality rate.[1] Cohen *et al* did publish a retrospective analysis of 130 aneurysms in which they noted a 1.5 percent mortality in those that were monitored with Swan-Ganz versus a 5 percent mortality in those monitored without.[3] In contrast, Pairolero reports 106 patients monitored aggressively and a mortality rate of 5.7 percent.[9] But when anesthetists were polled in a nationwide review by Hessel, a wide variation in usage of these catheters was noted.[4]

There is a question as well as to what use is made of the large amount of data generated in patients having routine Swan-Ganz catheter placement. Pierson and Funk looked at 33 consecutive post-op coronary artery bypass graft patients coming to the I.C.U. with indwelling lines in place.[5] In all of those patients, it was documented that clinical decisions regarding colloid and crystaloid administration were based on traditional measures of cardiac function including blood pressure, heart rate, urine output, auscultation of the lungs, chest Xray, oxygen saturation, etc. The extensive, carefully-recorded measures of cardiac output and wedge pressures in this group of elective patients were largely ignored.

Even without invasive monitoring of intra-cardiac pressures, today's anesthetists have a wide variety of parameters which are routinely monitored intra-operatively. These include ongoing E.K.G. and arrythmia detection monitors, S.T. segment monitors, temperature monitors, peripheral nerve stimulators, end-expiratory CO_2 levels, oxygen saturdation, in-line O_2 and NO_2, and agent specific monitors, automatic blood pressure determinations, airway pressure, and total volume monitors. In addition, the anesthetist has the benefit in our institution of a pre-operative cardiology consultation. When necessary, pre-operative stress tests, ejection fractions determined with nucleotide scans, and cardiac ultrasounds are carried out.

Pre-operatively our patients receive adequate hydration, antibiotic prophylaxis, and pulmonary toilet, and intra-arterial oxygen saturations. Intra-operatively the anesthetists measure blood losses accurately, including weighed sponges.

The single most important objective measurement of outcome in aortic surgery is probably the 30-day mortality rate for elective procedures. We believe that our 1.9 percent rate for elective aorto-iliac bypass compares quite favorably with the literature. With respect to elective aneurysms, a rate of 4.1 percent seems satisfactory, given the range reported in the literature. When these 6 deaths were reviewed, it appears unlikely that invasive monitoring would have altered the outcome in these particular patients. Two suffered sudden myocardial infarctions after 48 hours: in most centres the Swan-Ganz catheters are removed after 2 days, and so would not have been present in these patients. Three suffered multiple complications over a period of time and were, in fact, intermittently monitored with Swan-Ganz catheters. One patient suffered a massive stroke.

CONCLUSIONS

We find that an analysis of our results supports our belief that the routine pre-operative insertion of Swan-Ganz catheters is not necessary in patients undergoing aortic surgery. We would recommend that vascular surgeons renegotiate this item with their anesthetic departments. At the very least, the use of thermodilution catheters could be reserved for patients in the high risk categories. By doing so, we believe that those surgical departments will shorten the O.R. time for their patients, spare the patients the morbidity of this invasive technique, do something to help reduce hospital costs, increase the efficiency of the usage of O.R. time, and simplify the post-operative management of these patients in the intensive care units. We believe our data supports the contention that all of these things can be done without sacrificing anything in terms of quality care for our patients. □

ACKNOWLEDGEMENTS

The author wishes to acknowledge the partial support of Brent Surgical Corporation in chart review: Dr. Anitra Laycock for supplying relevant references; Mrs. Jan Terry for typing the manuscripts and documents: Mr. A. C. Watson of M.S.I. for supplying data regarding financial impact of Swan-Ganz monitoring; Mr. John Malcolm, Administrator of Health Care Institutions, Department of Health and Fitness, for supplying further data on the costs of invasive monitoring; and finally, to the Medical Records Department of the Sydney City Hospital for their cooperation and assistance in allowing us to complete the chart review.

References

1. Bashein MD, Johnson PW, Davis KB, Ivey TD, MD. Elective Coronary Bypass Surgery without Pulmonary Artery Catheter Monitoring. *Anesthesiology* 1985; **63**:451-454.
2. Calvin JE. Hemodynamic Monitoring: A Technology Assessment. *Can Med Assoc J* 1991; **145**:346-354.
3. Cohen JL. Hemodynamic Monitoring of Patients Undergoing Abdominal Aortic Surgery. *Am J Surg* 1983; **146**:174-177.
4. Hessel II, Eugene A. Intraoperative Management of Abdominal Aortic Aneurysms. *Surg Clin North Am* 1989; 69.

Continued on page 31.

Recommendations Concerning the Use of Folic Acid for the Prevention of Neural Tube Defects

A carefully controlled international study, sponsored by the British MRC, has shown beyond reasonable doubt that supplemental maternal folic acid ingestion during the periconceptual period is effective in reducing the risk of a fetal neural tube defect (NTD) in a subsequent pregnancy following the birth of an affected infant.[1] Results of this latest study (in which the Atlantic Research Centre collaborated) indicated that the risk was reduced by about 70%.

For a couple who have had a child with a neural tube defect but who have no other relevant family history, this means that the institution of an appropriate supplemental folic acid regimen in a future pregnancy would reduce their risk from around 4% to about 1%. (The Maritime population risk with no family history of NTD is 0.2%.)

The protocol we are now recommending for mothers carrying a risk of NTD on account of a previous affected pregnancy, calls for supplemental folic acid, 4 mg/day, commencing as soon as reliable contraception is discontinued (eg. on cessation of oral contraceptive regimen). The folic acid should be continued until a pregnancy is established and for the first 12 weeks of that pregnancy (the interim recommendation made by the US Centre for Disease Control is for the first three months).[2] A similar recommendation has also been made by the Maternal/Fetal Committee of the American College of Obstetrics and Gynaecology.

We suggest that this information be brought to the attention of all parents who have had a child with a NTD and who may be considering a future pregnancy.

The siblings of the parents of a child or pregnancy associated with a NTD also have a 1% risk of a NTD (five times the general population risk) in their potential offspring and we recommend consideration of maternal periconceptual folic acid for any pregnancies produced by these persons. Other pregnancies at increased risk of NTD include women with insulin-dependent diabetes and women with seizure disorders being treated with valproic acid. (Note that folic acid supplementation may upset anticonvulsant control in patients with grand mal epilepsy; we therefore recommend that such patients receive folic acid supplements under medical supervision.) In the case of all these individuals, supplemental folic acid in the amount of 1 mg/day is recommended, since there is strong evidence that this lower dose will also reduce the risk of NTD in these circumstances.

Physicians who prefer to refer their patients for genetic counselling through the clinical genetics service may do so by calling 494-6491. We would also be happy to offer advice or comment on those families with a more uncertain or complex history of a neural tube defect.

The Centre for Disease Control has recently recommended that all women of childbearing age in the United States who are capable of becoming pregnant should consume 0.4 mg of folic acid per day for the purpose of reducing their risk of having a pregnancy affected with spina bifida or other neural tube defect.[3]. The CDC considers that this amount of folic acid supplementation is more appropriate for the general population and in the belief that it is also effective in reducing the risk of NTD.

In summary, in order to *reduce* the risk of NTD, it is recommended that:

a) For women who have had a previous affected pregnancy – 4 mg of folic acid should be taken during attempts to initiate a pregnancy for the first 12 weeks of any ensuing pregnancy.

b) For other pregnancies at risk of NTD above that of the general population, including insulin-dependent diabetics, women on valproic acid, and women who have a close relative with a neural tube defect, folic acid supplementation of 1 mg/day, should be taken during attempts to initiate a pregnancy and for the first 12 weeks of any ensuing pregnancy.

c) For women in the general population, at low risk for neural tube defect, a daily supplement of 0.4 mg of folic acid should be taken during attempts to initiate a pregnancy and for the first 12 weeks of any ensuing pregnancy.

Physicians should recognise that the above regimens will not *eliminate* the risk of NTD or obviate the need for prenatal monitoring in appropriate instances. □

Nova Scotia Prenatal Diagnosis Group, A.C. Allen, MD; B.A. Armson, MD; M.J. Beis, MSc; B. St. J. Brown, MD; J.S. Calder, RN; E.B. Grantmyre, MD; R.M. Liston, MB; M.D. Ludman, MD; E.B. Pelausa, MD; L. Resch, MD; C.E. Smith, RN; D.A. Stinson, MD; D.L. Thompson, MD; M.C. Van den Hof, MD; J.P. Welch, MB; and P.C. Zimmer, MHSA.

References

1. MRC Vitamin Study Research Group. Prevention of neural tube defects. *Lancet* 1991; **338**:131-137.
2. Interim CDC recommendations for folic acid supplementation for women. *JAMA* 1991; **266**:1191.
3. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. *MMWR* 1992; **41** (No. RR-14):1-7.

Footnote:

Physicians should note that 1 mg and 0.4 mg tablets of folic acid may be obtained without a prescription (folic acid strength >1 mg requires a prescription).

Lithium Augmentation in Schizoaffective Depression

Richard J. Stern*, MB, ChB and Lakshmi N. Yatham**, MBBS, DPM, MRC Psych (UK), FRCPC

Halifax and Dartmouth, N.S.

The role of addition of Lithium in augmenting response to tyricyclic antidepressants in schizoaffective depression is described, and the possible biochemical basis for such response is suggested.

The indications for the use of lithium have been expanding ever since the observation by Cade in 1949 that lithium exerted a calming effect in animals that could be extended to humans. These indications can be divided into three main groups.[1]

As a primary agent, the use and efficacy of lithium in the treatment of mania is now firmly established.[2] It does have some therapeutic effect during depressive episodes, especially those occurring as part of a bipolar illness.[2] Its use has been described in a number of other conditions including alcoholism, impulsive-aggressive behaviour, premenstrual dysphoria and obsessive compulsive disorder.[3] Equivocal results have been reported on the effects of lithium in schizoaffective disorder .[4] It has been suggested that lithium either alone or added to a neuroleptic may be beneficial in schizoaffective mania.[6]

The prophylactic effect of lithium in bipolar disorder is one of the best documented in psychiatric pharmacotherapy.[6] Many studies show lithium to be equally effective as a prophylactic agent in unipolar depression.[7] The efficacy of lithium prophylaxis in schizoaffective disorder has been reported in those without prominent schizophrenic-like features. It was found to be more effective in schizomania and relatively ineffective in schizodepression.[8]

De Montigny C. *et al.* were the first to report the augmentation effect of lithium in tricyclic resistant depression.[9] Since then, other studies have confirmed these findings.[10] Lithium appears to augment the efficacy of almost all antidepressant medications and of carbamazepine in patients with unipolar, bipolar, and psychotic or non-psychotic depression.[11,12] The response is usually rapid, occurring within two weeks but may be delayed.[13]

To the best of our knowledge, lithium augmentation of tricyclic antidepressants has not been reported in the treatment of schizoaffective depression or major depression with mood incongruent psychotic features. We wish to report such a case.

* Resident, Nova Scotia Hospital, Department of Psychiatry, Dalhousie University, Halifax, N.S.

**Assistant Professor\Active Staff, Dept. of Psychiatry, Dalhousie University, Nova Scotia Hospital.

Correspondence: Dr. L.N. Yatham, Nova Scotia Hospital, P.O. Box 1004, Dartmouth, N.S. B2Y 3Z9

Case

Miss L. is a 23 year old, single woman who was admitted with a six-week history of auditory and visual hallucinations, bizarre delusions, delusions of guilt, and grandiose delusions. She appeared quiet, withdrawn, relatively inactive and exhibited poverty of speech with ambivalence. She reported her mood as anxious and depressed. She exhibited neurovegetativesymptoms of loss of appetite, weight loss, anhedonia, decreased energy, and diurnal variation in her mood.

At 19 years of age, she was seen in a psychiatric outpatient clinic, at which time she described bizarre ideation almost of a delusional nature. She had recurrent thoughts of inducing animals to have sex with people. These thoughts had been recurring over the previous three years, associated with occasional periods of dysphoria. A diagnosis of obsessive disorder with dysthymia was made and she was treated with clomipramine with no improvement in her symptoms. She relocated and was lost to follow-up until she was admitted to a large general hospital 18 months prior to her present admission. She described auditory hallucinations, delusions of persecution and guilt with mild dysphoric symptoms. A diagnosis of paranoid schizophrenia with dependent personality traits was made, and she was treated with chlorpromazine with some improvement in her condition. After her discharge, she was followed as an outpatient for six months, was intermittently non-compliant with her medication and, at times, exhibited a recurrence of psychotic symptoms and anxiety with no significant depressive symptoms.

Her birth and developmental milestones were normal. She attended school until the age of 16 years, reaching but not passing Grade 9. Previously, her school marks had been in the high 70s in Grade 7 but had significantly deteriorated over the next two years. She withdrew from school and remained at home for 18 months, unsuccessfully attempting a hairdresser course.Within the family, she was observed to be markedly dependent on her mother and possessive of her attention to the exclusion of her other siblings. She then relocated to a large city where she was employed in her elder brother's cleaning business until her first hospitalization.

There is a family history of her father suffering from recurrent major depression without psychotic features.

Routine investigations including CBC, renal, hepatic, and thyroid studies were normal. EEG, CT scan, and MRI brain scan were reported as normal. Neuropsychological testing was normal.

A diagnosis of schizoaffective depression was made and major depression with mood incongruent psychotic features was considered as part of the differential diagnosis.

She was commenced on haloperidol and imipramine on a gradually increasing dosage. As there was no significant improvement in her clinical condition after four weeks, the haloperidol was discontinued. She continued on imipramine and two weeks later, fluphenazine was added. This led to a significant improvement in her psychotic features by the tenth week of admission but she continued to remain depressed, anxious, and withdrawn, despite therapeutic levels of imipramine over an eleven-week period.

Lithium, 900 mg daily, was added at this stage to her treatment regimen. Within 3 to 5 days, her mood noticeably improved confirmed by self-report and staff observation. Although still quiet and relatively passive, she described feeling happier, more confident and motivated, with no further feelings of guilt. This improvement was maintained through the duration of her hospital stay of a further six weeks.

DISCUSSION

This case demonstrated the clinical usefulness of lithium in augmenting a tricyclic antidepressant in the treatment of schizoaffective depression.

Firstly, the issue of diagnosis warrants further discussion. This patient exhibited symptoms by the age of 16, with documented prior deterioration of functioning at school over two grade levels. There has been no sustained return to premorbid levels of functioning over the last seven years. She has exhibited bizarre delusions and hallucinations in the absence of prominent mood symptoms at various stages of her psychiatric illness. She has been treated at various stages with a tricyclic antidepressant alone, a neuroleptic alone and, most recently, a combination of tricyclic antidepressant and neuroleptic for more than six weeks at therapeutic levels without remission of all her symptoms. This seems to indicate that she had schizoaffective depression rather than major depression with mood incongruent psychotic features. However, in view of the family history of major depression and the pervasiveness of her affective symptoms at various stages of her illness, one could still consider the latter diagnosis. Her clinical improvement after 3 to 5 days of lithium treatment is consistent with earlier reports of rapid response to lithium augmentation for major depression refractory to adequate antidepressant trial.[9,10,14]

Lithium augmentation has been used successfully in the treatment of schizophrenia,[15] and psychotic depression refractory to combined antipsychotic-antidepressant treatment.[12] It was found to be a more effective treatment in patients with bipolar rather than unipolar-refractory psychotic depression.

The biochemical basis for the antidepressant effect of lithium hypothesized to be related to its ability to enhance 5-HT function by increasing the release of 5-HT into the synaptic cleft as well as by enhanced 5-HT postsynaptic receptor sensitivity.[14] Chronically administered antidepressant treatments, including drugs that block uptake of NE and 5-HT such as imipramine, cause subsensitivity of the NE sensitive adenylate cyclase and/or down regulation of beta adrenoceptors, which is considered to be an essential biochemical step in improving depressive symptoms.[16] Reduced serotonergic activity in some patients with refractory depression hinders such down regulation.[17,18] Thus, the well known enhancement of 5-HT function by lithium is believed to facilitate this down regulation of the NE beta adrenoceptor system, which correlates with the clinical response noted. The rapid improvement in depressive symptoms in our patient, following the addition of Lithium, seems to indicate that the depressive symptoms in schizo-affective depression may possibly have a similar biochemical basis as the depressive symptoms in major depression.

In addition to these proposed mechanisms, several other effects of lithium could be relevant, including enhancement of receptor sensitivity to other neurotransmitters and inhibition of formation of second messengers which may all have relevance in the pathophysiology of schizoaffective disorders.[19]

In conclusion, lithium was found to be very effective in enhancing the antidepressant effects of a tricyclic antidepressant in the treatment of schizoaffective depression. □

References

1. Cade JFB. Lithium Salts in the treatment of Psychotic excitement. *Med J Aust* 1949; **36:** 349-352.
2. Schou M. Lithium treatment. *Br J Psychiat* 1986; **149**: 541-547.
3. Jefferson JW, Griest JH, *Primer of Lithium Therapy*. Baltimore: Williams & Wilkins, 1977.
4. Miller FT, Libman H. Lithium carbonate in the treatment of schizophrenia and schizo-affective disorder: A review and hypothesis. *Biol Psychiat* 1979; **14**: 705-710.
5. Levison DF & Levitt ME. Schizoaffective mania reconsidered. *Am J Psychiat* 1987; **144**: 415-425.
6. Prien Robert F, *et al.* Drug therapy in the prevention of recurrences in unipolar and bipolar affective disorders. *Arch Gen Psychiat* 1984; **41**: 1096-1104.
7. Schou M. Lithium prophylaxis: Myths and realities. *Am J Psychiat* 1989; **146**: 573-576.
8. Maj M. Lithium prophylaxis of schizoaffective disorders: A prospective study. *J Affective Disord* 1988; **14**: 129-135.
9. De Montigny C, Grunberg F, Mayer A, *et al.* Lithium induces rapid relief of depression in tricyclic anti-depressant drug non-responders. *Br J Psychiat* 1981; **138**: 252-256.
10. Price LH, Charney DS, Heninger GR. Variability of response to lithium augmentation in refractory depression. *Am J Psychiat* 1986; **143**: 1387-1392.
11. Kramlinger KG, Post RM. The addition of lithium to carbamazepine; Antidepressant efficacy in treatment resistant depressions. *Arch Gen Psychiat* 1989; **46**: 794-800.
12. Nelson JC, Mazurre CM. Lithium augmentation in psychotic depression refractory to combined drug treatment. *Am J Psychiat* 1986; **143**: 363-366.
13. Dallal A, *et al.* Lithium carbonate augmentation of desipramine in refractory depression. *Can J Psychiat* 1990; **35**: 608-611.
14. De Montigny C, Cournoyer G, Morissette R, *et al.* Lithium Carbonate addition in tricyclic-antidepressant resistant unipolar depression. *Arch Gen Psychiat* 1983; **40**: 1327-1334.
15. Jefferson JW. Lithium: The present and the future. *J Clin Psychiat* 1990; **51**: (8 suppl), 4-8.

Continued on page 31.

Incidences of Asthma and Bronchitis in a Group of Young Male Hockey Players

A PILOT STUDY

T. W. Pelham,* MSc

Halifax, N.S.

The survey-based study found 16% out of 205 young male hockey players with physician-diagnosed asthma. 72% of these asthmatics took medication to prevent or for relieve from an exercise-induced episode (pre/rel-EIE). Although, there were more asthmatics in the older age groups than the younger, more of the younger asthmatic players were on medication (pre/rel-EIE) than the older players. Conversely, the incidence of physician-diagnosed bronchitis was lower in the youngest age group and higher in the older groups. When considered together, the incidence of physician-diagnosed asthma and bronchitis (AB) was 18% and those in the pre/rel-EIE, represented 75% of those afflicted. There was a higher incidence of AB among players with 5 or more years of experience in organized hockey (18%) than in the group with 4 or fewer years (15%).

A discussion on the possible high risk features of the indoor environment of the hockey rink for asthma and bronchitis follows.

Asthma has been characterized by attacks of wheezing and labored breathing resulting from spastic contractions of the bronchiolar smooth muscle, localized mucosal edema in the walls of the small bronchioles and secretion of thick mucus into the bronchiolus lumens.[1] During an asthma attack the bronchi are constricted, reducing bronchiolar diameter and increasing airway resistance. Airway obstruction is increased during expiration occlusion.[1] As a result, expiration becomes uncomfortable work leading to ventilatory insufficiency, and dyspnea.

Asthma is a disease that begins early in life and is a major health problem in childhood. Although asthma sometimes lessens in severity or disappears completely as a person grows older, it has been suggested that there are 140,000 asthmatic children below age 15 in Canada.[2] Indeed, since 1970 asthma death rates among young Canadians have tripled and hospital admissions have increased sharply for Canadians below the age of 15.[2]

Although the causative factors for asthma are controversial, several causal relationships (triggers) have been suggested.[1-3] These are allergic hypersensitivity of the bronchioles to airborne allergens, such as, plant pollen, mold and animal hairs, environmental pollution, for example, emissions of carbon monoxide, nitrogen oxides, sulphur oxides, active hydrocarbons and particulates from mobile-source pollutants, respiratory infection, familial predisposition, cold, exercise and emotion.

Bronchitis is another chronic obstructive pulmonary disease. In bronchitis, there is a chronic inflammation of the airways, and mucus overproduction obstructs the airways, interfering with adequate oxygen supply (hypoxia/hypoxemia) and carbon dioxide removal (hypercapnia).[3] As was the case for asthma, by-products of combustion (nitrogen oxides, sulphur oxides and carbon monoxide)[4] are irritating to the airways of a person with bronchitis.[3]

As mentioned, asthma attacks might be precipitated by participation in strenuous physical activities. Such an asthmatic episode is referred to as an exercise-induced bronchospasm/bronchoconstriction (EIB) or exercise-induced asthma (EIA). Controversy surrounds EIA as to whether it is life-threatening.[5,6] Although the underlying causes of EIA are not fully understood, one hypothesis suggests that changes in airway temperature and humidity by exercise-induced hyperpnea and exercise-induced bronchomotor tone, as well as exercise enhanced airway secretions trigger EIB.[6] Environmental determinants such as breathing cold, dry air with a high exposure of ambient air pollutants have been suggested to enhance EIB.[6]

EIB may also occur in the swollen and inflamed airways of a person with bronchitis. Premedication serves to protect against EIB and premature dyspnea when severe obstruction exists.[3]

In respiratory research, attempts have been made to identify high risk environments for asthmatics and persons with bronchitis. One line of research has focused on the indoor living environments of asthmatics and persons with bronchitis. For example, the living quarters of asthmatics are currently under intense investigation.[7] However, another indoor environment with the potential for triggering asthma or bronchitis, and therefore at high risk is the indoor hockey rink.

Indoor commercial rinks operate for 11 months, with a shutdown in the spring for maintenance. To reduce high operating costs rinks usually are not heated. Indeed, in freezing and maintaining a hard sheet of ice suitable for hockey, an overall brine temperature of -10°C is required.[8] To maintain low ambient air temperatures, many rinks install additional insulation to minimize ventilation. However, reducing air exchange may increase the concentration of indoor pollutants.

Ambient air pollutant concentration has the potential to be an important feature in determining risk level.

*Exercise Physiologist, Athletics and Recreational Services, Dalhousie University.

Correspondence: T. W. Pelham, Dalplex, South Street, Dalhousie University, Halifax, N.S. Canada B3H 3J5

There are four likely sources of air pollutants in the hockey rink:

1) the gas-driven resurfacing machine (see above mentioned pollutants),
2) rink fog and ceiling dripping (dampness for mold growth),
3) food and drink debris (nutrients for mold colonization),
4) chemical vapors for the refrigeration system.

From the above, therefore, it seemed important to establish if the indoor hockey rink is suffering from the "sick building syndrome". Consequentially, several objectives can be established:

1) to identify the incidences of asthma and bronchitis among young hockey players,
2) to determine to what extent EIB is present among young asthmatic hockey players and players with bronchitis,
3) to identify possible sources of pollutants for pollutant-induced asthma and pollutant-induced bronchitis in a hockey rink.

SUBJECTS AND METHODS

In a survey of 205 young (range: 8-15 years of age) male, hockey players, attending a hockey skill camp, a series of questions was asked related to respiratory illness and how long each subject had played organized hockey.

Children were classified into one of the following three groups:

1) *Physician-diagnosed asthma:* Children were identified as currently asthmatic if they answered yes to the question; "Has a medical doctor recently said you have asthma?"
2) *Physician-diagnosed bronchitis;* Children were identified as suffering from bronchitis if they answered yes to the question; "Has a medical doctor said you have bronchitis."
3) *nondiagnosed:* All the remaining children were grouped together. The label of nondiagnosed was used in an attempt to recognize that there is a possibility that some of the children in the sample may have asthma or bronchitis, but not diagnosed by a physician, or another chronic obstructive pulmonary disease ignored by the survey, for example, emphysema.

Subsequently, when a child answered yes to either question 1, or 2, they were asked if they were given prescription drugs from a physician for their respiratory condition. For children requiring medication, the frequency of use, and if they took the medication before, during or after exercise or playing hockey, was requested. It was assumed that children requiring medication before, during or after strenuous activity were prone to EIB and the medication was used to prevent or relieve an exercise-induced episode (pre/rel-EIE).

In addition, age and the number of years of participation in organized hockey were recorded.

RESULTS

Table I shows that hockey players have higher incidences of asthma than the general population of Canada for each age group investigated. Indeed, the overall incidence of asthma was 16% (32/205), compared with the national average from children of 7-10%.[9] The overall incidence for bronchitis was lower, 2% (4/205) versus the national average[2] for children, 3.4%, as were the incidences of bronchitis for each age group compared with the general population of Canada (Table I). Table I also shows that there were more asthmatic hockey players and players with bronchitis in the older age groups than the youngest group.

23 of the 32 asthmatics (72%) reported pre/rel-EIE. Estimates for EIA among male asthmatics have been reported between 70-80%.[10] While Table II shows that more of the younger asthmatic players (5-9 age group) were on medication (pre/rel-EIE) than the older players (10-14 and 15 year olds), older players with bronchitis were more prone to pre/rel-EIE than younger subjects.

When considering that 4 individuals in the sample reported physician-diagnosed bronchitis, the overall incidence of asthma and bronchitis (AB) was 18% (36/205) and those in the pre/rel-EIE represented 75% (27/36) of those afflicted. In Table III, there was a higher incidence of AB among players with 5 or more years of experience in organized hockey (18%) than in the group with 4 or fewer years (15%). However, pre/rel-EIE in the older players was 75%.

TABLE I

COMPARISON OF THE INCIDENCES OF ASTHMA AND BRONCHITIS IN CANADIAN CHILDREN UNDER THE AGE OF 15 WITH THE INCIDENCES AMONG MALE HOCKEY PLAYERS UNDER THE AGE OF 15

Condition	Age Groups		
	5-9	10-14	15
Asthma			
Canadian population*	3.9**	4.4	NA
hockey players††	5†	16	29
Bronchitis			
Canadian population*	4.0**	3.4	NA
hockey players††	0.0†	2	7

* Statistics Canada. 1986. *Report of the Canadian Health and Disability Survey 1983-1984.* Ottawa: p. 107.
** Percentages are expressed as a proportion of the total Canadian population of that age group.
† Percentages are expressed as a proportion of the total sample size of that age group.
†† Sample did not include 5, 6, or 7 year old hockey players (no data collected).

TABLE II

INCIDENCES OF PRE/REL-EIE IN ASTHMATIC HOCKEY PLAYERS AND IN PLAYERS WITH BRONCHITIS FOR THAT AGE GROUP (N = 32).

Age Groups	Asthma percent*	Bronchitis percent*
5-9	100	0.0
10-14	70	100
15	75	100

* Percentages are expressed as a proportion of the total number of asthmatics or subjects with bronchitis for that age group.

TABLE III

DISTRIBUTION OF ASTHMATICS AND SUBJECT WITH BRONCHITIS BASED ON EXTENT OF INVOLVEMENT IN ORGANIZED HOCKEY (N = 205).

Years in Organized Hockey	Asthma percent*	Bronchitis percent*	Both percent*
5 or more	16	2	18
4 or fewer	15	0.0	15

* Percentages are expressed as a proportion of the total sample size.

DISCUSSION

Asthma is a major illness of childhood. Bronchitis is another serious illness and can lead to, or be associated with pulmonary emphysema.[3] In fact, and somewhat disturbing, this study has found a higher incidence of asthma among hockey players than in the general Canadian population. There were more asthmatics in the older age groups than the youngest. However, more of the younger asthmatic players were on medication (pre/rel-EIE) than the older players. There was a higher incidence of AB among players with 5 or more years of experience in organized hockey than in the group with 4 or fewer years. Yet the incidence of pre/rel-EIE among asthmatic hockey players was within the estimates for the larger Canadian male asthmatic population for these age groups.*

Although certain drugs (beta$_2$-adrenergics, corticosteroids, Cormolyn Sodium and Theophylline) are used to prevent EIA,[6] identifying potential hazards in the exercising environment is an important consideration in asthma and bronchitis management.

The most common trigger of EIB is exercising in a cool, dry environment.[6] Studies have also suggested that exposure to indoor contaminants, such as nitric oxide from gas cooking,[7] environmental tobacco[2] and airborne particulars from mold colonies[1] increases the risk of respiratory illness. Consequently, internal environments where individuals are spending long periods of time, where there is a reduction in the exchange of air and high concentrations of indoor pollutants, a profound risk of aggravation of pulmonary dysfunctions exists.

There are several uncontrolled factors in this study. The survey ignored the incidences of allergies and other respiratory conditions, as well as other conditions (eg., outdoor environment) potentially responsible for triggering asthma or bronchitis or EIB. The medical history of the asthmatics and subjects with bronchitis, the lifestyles, geographic residence and social backgrounds of the subjects were also not identified. In addition, pinpointing the subject's home rink and distinguishing the air composition of these rinks may provide valuable information. The survey-based study likewise encompassed only a small sample of the male hockey population of Nova Scotia. Nevertheless, the results of this pilot study serves notice that asthma may be a common disease among young hockey players in the province of Nova Scotia.

Although proof of efficacy is lacking, two important questions must be asked: "Is there a higher probability of an experienced hockey player having asthma than a young individual who does not play organized hockey and, if so, why? Answering these questions is beyond the scope of this discussion, however, presenting hypotheses and recommendations may be fruitful for future research. To begin with the second question, as mentioned earlier, the hockey rink is an intentionally enclosed environment. Temperatures are maintained below freezing and the air is dry. The activity performed by the athlete is strenuous, and hyperpnea is common. Emotions are high during a game, especially with children. Indeed, the majority of factors conducive to an asthma episode are present.

Other possible inducing agents, or triggers for asthma and bronchitis are high concentration of ambient air pollutants. Mentioned earlier were four possible sources of pollutants. Of those, the most consistent source, therefore the most likely candidate, is the exhaust from the resurfacing machine. All rinks use these machines. Not all rinks have leakage problems and most are clean. In addition, government regulations for refrigeration are such that the probability of leakage from the rink's cooling system is minimal.

There are several motives for considering the resurfacing machine as a major indoor pollutant. During resurfacing, these machine are always accelerating and decelerating, they seldom idle or cruise. During acceleration and deceleration, the internal combustion engines of these machines release greater amounts of carbon monoxide, nitrogen oxides, sulphur oxides, unburnt hydrocarbons and particulates than at times of idling or cruising.[4]

Compounding this situation is the behavior of the players. Many players skate onto the ice surface just as the resurfacing machine has finished. At this time, the pollutants are at their greatest concentration. In addition, the players on both teams are emotionally ready to play and

* This discussion assumes that the use of medication before, during or after exercising is the sole treatment prescription for prevention or relieve of EIB/EIA.
However, medication taken at other times may, in fact, have a preventive effect, suggesting a higher incidence of EIB/EIA among young male hockey players.

reflect this by skating with great velocity many times around the rink, raising their ventilation, and shouting encouragement to teammates. This activity, creates a high risk condition for an asthma attack or bronchitis-associated EIB.

Another feature concerns the architecture of many community-based rinks. With limited construction budgets, many rinks have low ceilings allowing the pollutants to accumulate near the ice surface. Indeed in many rinks, the garage for the resurfacing machine is next to a dressing room, or the entrance to the ice surface, increasing the exposure to the pollutants.

Most important, many of these pollutant remain in the ambient air. The combination of reduced air exchange, cold temperature, lack of sunlight, and low humidity suggest that the only intermediate reactions for these pollutants are through oxidation with ambient oxygen.* These secondary products are equally toxic.[4] Inadequate ventilation may allow an increase in concentration of these contaminants, in essence creating a high risk environment. In fact, the combination of severe exercise, adrenalin producing emotion of the game and the toxic environment may have a greater inducing effect for an episode than any of the individual triggers.

It is recommended that further, more controlled experimentation be carried out. The indoor environment of the hockey rinks of Nova Scotia should be scrutinized, and if high concentration of contaminants are present, steps must be taken to correct the situation. Larger, more complete surveys of the hockey population should be undertaken to investigate the incidences of chronic obstructive pulmonary diseases in various subgroups of the hockey population. Only then, can answers to the true incidences of asthma, bronchitis and other chronic obstructive pulmonary diseases among hockey players emerge.

Finally, in closing, it is important to note that although environmental and health concerns exist in one sporting activity, all health professionals should take leadership roles, encouraging children with asthma or bronchitis to exercise. Exercise, sport and recreational activities can potentially help the children's psychosocial development, as well as their somatic health. By not excluding the child with a chronic pulmonary disease from health-promoting exercise and sports (activities) the implications for a positive quality of life are enhanced. Indeed, by assuming an aggressive role in promoting physical activity the health professional helps to ensure that the child can reach his or her full functional potential. □

*The primary pollutants, sulphur dioxide and nitric oxide, are oxidized by ambient air (oxygen) to sulphur trioxide and nitrogen dioxide, respectively.[4]

$$2\,SO_2\,(gas) + O_2\,(gas) \rightarrow 2\,SO_3\,(gas)$$
$$2\,NO\,(gas) + O_2\,(gas) \rightarrow 2\,NO_2\,(gas)$$

References

1. Guyton AC. *Textbook of Medical Physiology* (8th Ed.). Philadelphia: W. B. Saunders Company, 1991.
2. National workshop on asthma: Executive summary and recommendations, Ottawa, May 19, 1988. *Chronic Dis Can* 1989; **10**: 33-34.
3. Haas F, Haas SS. *The Chronic Bronchitis and Emphysema Handbook.* New York: John Wiley & Sons, Inc., 1990.
4. Manahan SE. *Environmental Chemistry* (4th Ed.). Boston: PWS Publishers, 1984.
5. McFadden ER. Fatal and near-fatal asthma. *New Engl J Med* 1991; **324**: 409-411.
6. Stamford B. Exercise-induced asthma. *Phys Sportsmed* 1991; **19**: 139-140.
7. Dekker C, Dales R, Bartlett S, *et al.* Childhood asthma and the indoor environment. *Chest* 1991; **100**: 922-926.
8. American Society of Heating Refrigerating and Air-conditioning Engineers. *ASHRAE Handbook Refrigeration Systems and Application* (S1 ed.). Atlanta: Author, 1990.
9. Mao Y, Semenciw R, Morrison H, *et al.* Increased rates of illness and health from asthma in Canada. *Can Med Assoc J* 1987; **137**: 620-624.
10. Goldberg B. Children, Sport, and Chronic Disease. *Phys Sportsmed* 1990; **18**: 45-56.

GESTATIONAL TROPHOBLASTIC DISEASE REGISTRY

Continued from page 13.

If chemotherapy was required for low risk trophoblastic disease follow-up is as follows:

a) HCG weekly until three consecutive normal values are obtained. Then . . .
b) HCG monthly for one year. Then . . .
c) HCG once every three months for one year. Pregnancy is permissable after one year of normal titres. If pregnancy is suspected an ultrasound is indicated for early confirmation.

If chemotherapy was administered for high risk trophoblastic disease follow-up is as follows:

a) HCG weekly until three consecutive normal values are obtained. Then . . .
b) HCG once a month for two years. Pregnancy is permissable after two years of normal titres. Once again, if pregnancy is suspected an ultrasound is indicated.
c) HCG once every three months for the third year.
d) HCG titres once every six months for the fourth year.
e) Yearly thereafter. □

ACKNOWLEDGEMENT

Our sincere thanks for the continued support of the patients, physicians and pathologists.

What is the Matter with Claudius?

George M. Burden, MD

Elmsdale, N.S.

The Emperor Claudius, the fourth to rule Rome, succeeded to the throne after the assassination of Caligula in AD 41 at the age of fifty. He is known to the general public through the novels of Robert Graves and the award winning television series, "I Claudius", based on the works of the aforementioned author. Though treated unkindly by his posterity, it would appear that he was in fact an able and effective administrator in many ways and ruled well during his thirteen years tenure. Nevertheless he was haunted by a curious stigma which caused his own mother to describe him as "a monster, a man whom nature had not finished yet merely begun". His family in fact, after deliberation, decided to hide him from public scrutiny as an embarrassment to the Julio-Claudian clan (the ruling family related to Julius Caesar). Augustus himself described Claudius as being "defective in soundness of body and mind". This problem seemed to develop at an early age and was the cause of much ridicule to the young Claudius. But what was its nature?

Physically, the historian Suetonius, describes the Emperor as "tall, well built, with a handsome face, a fine head of white hair and a firm neck". Furthermore, Claudius was of superior intellect. Because of his early deprivation of a public life, he composed many literary works including a twenty volume history of the Etruscans and an eight volume history of Carthage which were well received in Roman intellectual circles. In fact, the famous museum in Alexandria even named a wing after the scholarly Emperor.

Why then was the future Emperor such an outcast in early life, and continued to be ridiculed even after assuming Imperial honors? Being of good intellect and a handsome appearance, the only alternative explanation is a behavioral abnormality and one not under good voluntary control by its victim.

Suetonius goes on to further describe Claudius as having "several disagreeable traits . . ., an uncontrolled laugh, a horrible, habit, under stress or anger, of slobbering at the mouth and running at the noise, a stammer and a persistent nervous tick of the head which was apparent at all times but especially when he exerted himself to the slightest extent." When Claudius was young the Emperor Augustus, in a letter, refers to the young lad's "capriciousness . . . in his movements, gait and deportment".

The Emperor was noted for his inappropriate remarks "such as would have come ill even from a private citizen". On one occasion he interrupted a solemn debate in the senate on the subject of butchers and wine merchants with the comment "how can anyone live without an occasional snack?". It was further remarked that "every day and almost in every hour he would let fall such remarks as 'What? Do you take me for (fool)?' 'Very well, curse me if you will but keep your hands off!'".

Despite the chronic nature of his impediments Claudius seemed to be able to suppress these tics and inappropriate verbalizations for at least a period of time. Augustus once exclaimed of him "confound me . . . how in the world anyone who is so unclear in his conversation can speak with clearness and propriety when he declaims is more than I can see".

We are faced therefore with a man, sound of appearance and intellect, and indeed the capable administrator of a vast Empire, who invokes ridicule because of his unpredictable and inappropriate verbalizations and tics which nevertheless he seems to be able to temporarily suppress. This is highly suggestive of a diagnosis of Tourette's syndrome.

Claudius' tics were primarily of the head and neck, the most common location in Tourette's, affecting 94% and 91% of sufferers respectively in these areas. Stuttering and stammering are noted to be seen in 20% of Tourette's patients, occurring because of thoracic, abdominal or diaphragmatic muscle contractions. The Emperor's bizarre and inappropriate comments fit in with the compulsive need in some Tourette's sufferers to indulge in more complex vocalizations, as opposed to the sharp barks, grunts and coprolalia which do not seem to be ascribed specifically to Claudius. (Though the fact that his remarks "would have come ill from a private citizen" suggest that some coprolalia may indeed have been

present). The historians also found it notable to remark on Claudius' compulsive eating, gambling and womanizing habits.

The Emperor also showed signs of impulsiveness and irritability which can be associated features of Tourette's. Of course one would also wonder how much of a mental toll the affliction took and how much irritability would arise from simple frustration. The Emperor seemed to be very irascible later in his reign delighting in executions and punishing supposed slights rather arbitrarily and severely. He spent much time in the law courts and it was felt that his verdicts were sometimes rather impulsive, sometimes being very wise and sometimes being frivolous. For example, on one occasion a woman refused to acknowledge maternity of her adult son. Claudius suggested that they therefore be married on the spot at which point it became evident that the woman was in fact the young lad's mother. On the other hand he would often order executions on very scant grounds. Perhaps some of his irritability was due to the constant promiscuity of his wife, Messalina. On one occasion she engaged in a contest with a notorius prostitute to see who could "entertain" the most men in one evening. The Empress won. Subsequently she *publicly* married while her husband was out of the city. She was executed for her troubles as was her bridegroom.

The unfortunate sequel to this was that Claudius married his niece Agrippina and adopted her son by a previous marriage. Perhaps worn out by the disabilities and stigma attached to his Tourette's, his judgment was failing in his later years. In any event, after dining on poisonous mushrooms provided by his wife, the Emperor died miserably in AD 54 at the age of 64 years. This left the way clear for the "enlightened" rule of his adopted son Nero. □

References

1. "The Twelve Caesars" by Suetonius (*ca* 69 – *ca* 122).
2. Murray TJ. The Treatment of Tourette Syndrome *NS Med Bull* 1983; **62**:117-119.
3. "The Twelve Caesars" by Michael Grant.
4. "The Emperor Claudius" by Vincent M. Scaramuzza

Current Topics in Community Health

By: Susan A. Kirkland, MSc
Department of Community Health & Epidemiology
Dalhousie University, Halifax, N.S.

CORONARY HEART DISEASE: A FEMALE PERSPECTIVE

Coronary heart disease (CHD) is a major public health concern throughout industrialized nations, despite the fact that its mortality rates continue to decrease over time. Within Canada, Nova Scotia is recognized as having one of the highest rates of CHD for both males and females. The most recent data from Health and Welfare Canada report age-standardized mortality rates for ischemic heart disease in Nova Scotia to be 222 per 100,000 males and 108 per 100,000 females.[1] From these numbers alone, it is easy to see why heart disease has traditionally been considered a "male dominated" disease and research has largely been confined to one gender. Yet, heart disease is the leading cause of death for women as well as men, contributes the greatest amount of potential years of life lost for women as well as men, and results in longer hospital stays for women than men.[2]

Epidemiological data for coronary heart disease highlight significant differences between males and females, one of the most obvious being the age at which heart disease strikes. In men, mortality rates increase steadily from age 35 to age 60, at which point they begin to level off. In women, a sharp increase is not observed until after age 50, but the rates continue to increase past age 70. A number of explanations have been postulated to account for these gender differences: 1) a different presentation of the disease in women and men; 2) a lower prevalence of risk factors in women than men; 3) better tolerance of risk factors in women than men; and 4) protective hormonal and metabolic mechanisms unique to women.

There is evidence to suggest that heart disease does present differently in males and females. The common clinical manifestations of CHD are myocardial infarction (MI), angina, and sudden death. Men most often present with myocardial infarction as the first manifestation of disease, whereas angina is by far the most frequent symptom in women, accounting for greater than 50% of first clinical events.[3] When infarction does occur, women are more likely to have a prior history of angina, hypertension, or diabetes. The post-MI prognosis for women is also worse: in-hospital mortality and 30-day mortality among hospital survivors is significantly higher in women than men, and age alone cannot explain the difference.[4] After discharge, women more frequently experience recurrent angina, congestive heart failure, and reinfarction than men. Moreover, women are less likely to be candidates for surgical interventions such as bypass surgery and angioplasty and, when they are, their outcome is markedly less favourable.

The fact that angina is the predominant symptom of CHD in women raises some interesting points. First, many studies discount the presence of angina as an indicator of CHD because of the difficulty of measuring it. Indeed, it is often considered a "soft" endpoint when compared with other more quantifiable outcomes such as MI or sudden death. Since angina is not well reflected in mortality statistics and since it is rare to get population-based statistics of heart disease morbidity, we may be underestimating the extent of the problem in women.

Determining the correct cause of recurrent chest pain or discomfort can be difficult in women. Studies relating chest pain to coronary artery atherosclerosis show that all subgroups of men referred with chest pain have a greater than 50% prevalence of coronary stenosis, whereas only those subgroups of women with Canadian Heart Association class III and IV angina have a similar prevalence of stenosis.[5]

Bayes theorem relates the sensitivity and specificity of a diagnostic test to the overall prevalence of CHD in the population. Criteria for the diagnosis of CHD by non-invasive procedures, such as the treadmill stress test, have been derived in men. The lower prevalence of CHD in women, particularly those under 50, reduces the diagnostic value of the test, and increases the likelihood of false-positive results. This does not mean that chest pain in women should be dismissed, but rather that test results should be considered within the context of clinical features described: age, known risk factors, and in conjunction with further diagnostic testing whenever doubt remains.

It is generally accepted that the three main risk factors for heart disease – high blood cholesterol, high blood pressure, and smoking – are common to men and women, but the expression of these risk factors has been found to differ. For example, high density lipoprotein (HDL) cholesterol has been shown to be a stronger predictor of CHD in women than men, but total cholesterol and low density lipoprotein (LDL) cholesterol appear to be weaker risk factors for women than men. The role of hypertriglyceridemia as a risk factor for CHD is controversial. In studies where multivariate analysis has been conducted, plasma triglyceride level is usually found to be insignificant as an independent predictor for CHD events, and largely assumed to be the result of a concomitant interaction with low levels of plasma HDL. According to data from Framingham, however, hypertriglyceridemia remains as an independent risk factor for CHD in women, but not in men.[6]

Experience from the Framingham cohort has pointed to systolic blood pressure, blood glucose intolerance

and/or diabetes, and excess weight as having greater impact for CHD in women than men. Diabetes increases the risk of CHD 3-fold in women, resulting in the same risk level as age-matched non-diabetic men. Because the incidence is greater among women than men, and the death rate from MI is greater in diabetic women than men, early recognition is viewed to be important. Obesity and overweight are thought to play a mediating role through risk factors such as diabetes and low plasma HDL levels. Socioeconomic status appears to have an impact on obesity: excess body weight is reported to be more frequent in women of low versus high socioeconomic status.

Other risk factors, such as oral contraceptives and postmenopausal hormone use, are entirely unique to women. Estrogens tend to raise the plasma levels of HDL, whereas progestins tend to have the opposite effect. Relatively high doses of both estrogen and progesterone are thought to account for the increased risk observed in early studies of oral contraceptive use. On the other hand, postmenopausal estrogen replacement therapy has been shown to confer a protective effect on heart disease in women, the order of magnitude being a 30-50% reduction in risk. As a caveat, the optimal estrogen dose has yet to be determined, and the efficacy of concurrent use of progestins remains to be clarified.

At a population level, the key to disease prevention is risk reduction. Reducing the risk of coronary heart disease in women may be particularly important, given their less favourable prognosis and increased disability after MI. Knowledge of the prevalence of risk factors is useful in guiding population interventions, and we are fortunate to have the results of a population-based survey of risk factors in the province – the *Nova Scotia Heart Health Survey*[7] – conducted in 1986. The three primary risk factors appear to be as prevalent in women as they are in men overall, though trends may differ in relation to age. Thirty-one percent of Nova Scotian women aged 35-64 have an elevated serum cholesterol level (>5.2 mmol/L), but the prevalence increases to 57% in women aged 65-74. The prevalence of hypertension (>90 mmHg and/or on treatment) increases from 21% in women aged 35-64 to 50% in women aged 65-74. The prevalence of smoking decreases from 27% in women aged 35-64 to 12% in women aged 65-74, but shows alarming increases in prevalence in women of younger ages (currently 42% in women aged 18-34). A total of 73% of Nova Scotian women possess one or more risk factors for coronary heart disease.

Unfortunately, scientific research pertaining to coronary heart disease prevention has been carried out almost exclusively in male subjects. Recommendations for intervention in women have been directly extrapolated from these findings, despite uncertainty as to whether or not this is a valid generalization. For example, studies in middle aged males with hypercholesterolemia have documented that a reduction in total blood cholesterol is accompanied by a decline in CHD events, but this has not yet been shown directly in women. The benefit of antihypertensive medication in males has also been clearly established, yet a recent review of clinical trials of hypertensive therapy in women reaches a disturbing conclusion: the trials show clear benefit of therapy for black women but no clear benefit for white women, and some studies go so far as to suggest that treatment of white women is harmful.[8] The logistics of obtaining adequate numbers of events in women to achieve statistical significance has hampered the inclusion of women in many studies.

On a more positive note, there is growing recognition of the importance of coronary heart disease as a health issue for women. Given the magnitude of the problem in both women and men, population-based approaches to risk reduction and coronary heart disease prevention are warranted. The challenge will be to develop strategies which incorporate what we know about heart disease in women, and to promote research initiatives in those areas where evidence is lacking. □

References

1. Labratory Centre for Disease Control, Health and Welfare Canada; Canadian Centre for Health Information, Statistics Canada, 1990.
2. Johansen H, Nargundkar M, Nair C, *et al.* Women and cardiovascular disease. *Chronic Dis in Can* 1990; **11**:41-47.
3. Murdaugh CL, and O'Rourke RA. Coronary heart disease in women: special considerations. *Curr Probl Cardiol* 1988; **13**:73-156.
4. Peberd MA and Ornato JP. Coronary artery disease in women. *Heart disease and stroke* 1992; **1**:315-319.
5. Eaker ED, Packard B, Wenger NK, *et al.* Coronary artery disease in women. *Am J Cardiol* 1988; **61**:641-644.
6. Castelli, WP. The triglyceride issue: A view from Framingham. *Am Heart J* 1986; **112**:432-437.
7. Nova Scotia Department of Health and Department of National Health and Welfare. Report of the Nova Scotia Heart Health Survey Halifax, 1987.
8. Anastos K, Charney P, Charon RA, *et al.* Hypertension in women: What is really known? *Annals Int Med* 1991; **115**:287-293.

"Never believe what a patient tells you his doctor said."

Sir William Jenner (1815-98)

Medical Humanities

T. J. Murray, OC, MD, FRCPC

Halifax, N.S.

"The initial training of physicians is, all too often, it seems to me, deficient on the side of the Humanities. It is not enough for universities to train medical students in basic science and in technique. The must be more than technicians. They should read foreign languages. They should be able to express themselves in good English. They should read it and write it. They should learn to enjoy some aspect of literature, have some hobby in the Arts. These are not undue requirements for a person who is to be the spiritual councellor to educate men and women as well as keeper of their bodies."

Dr. Wilder Penfield

NOTES

MEDICAL SCHOOL APPOINTS ARTIST IN RESIDENCE

Following the Year of Medicine and the Humanities at Dalhousie Medical School in 1991, and during the Year of Medicine and the Environment in 1992, the Medical School has appointed an Artist in Residence, Verle Harrop.

Verle Harrop fuses satellite views of the planet with CAT and MRI images of the brain, creating spectacular large works made of brilliantly colored textiles. Speaking to *Dalhousie News*, she said, "I think one of the exciting things is that these are images of our lifetime. Prior to this we didn't have these images and so to deal, not only with the images, but also with the technology that produces them, is a very exciting challenge."

Harrop's work has been shown nationally and internationally, and will be seen in many shows over the next two years, including medical meetings.

As the Artist-in-Residence, she participates in the medical school programs and student events. Her term is for two years and during that time she will create further works including a new series that brings together the concept of disruption of borders in understanding the brain and in national relationships. For this series she has superimposed brain images on atlas maps of countries at the turn of the century.

MEDICINAL PLANTS ON THE MSNS GROUNDS

Next time you are wandering the Society's grounds, have a look to see how well the medicinal plants are faring. Dr. Ian Cameron, President of the Dalhousie Society for the History of Medicine, and aided by an able and informed band of interested growers, planted several local plants and trees on a nature trail around the beautifully shaped hill where the Society's new building sits. There is Labrador tea (asthma, common cold, kidney disorders), white spruce (colds, cough, grippe) Choke cherry (diarrhea), bunchberry (epilepsy), and yarrow (colds, swelling, bruises, sprains) and many opthers.

There are many medieval compendiums of herbal remedies, and the wonderful book by Culpeper, but the most interesting local interest is in the Micmac medicines, and the herbal therapies of the early physicians who came to the shores of Nova Scotia.

DALHOUSIE SOCIETY FOR THE HISTORY OF MEDICINE

For more than a decade the Dalhousie Society for the History of Medicine has been holding four informal dinner meetings at the Dalhousie Faculty Club, with two or three papers each evening. Some national representatives of medical history have suggested we have at Dalhousie one of the most active medical history societies in North America. It certainly is active and it certainly is interesting. I have attended almost every meeting over the years and I have not yet attended one that wasn't stimulating and interesting. If you don't belong (the dues are $10. – when did you last belong to anything with an annual dues of $10) call Dr. Ian Cameron, and arrange to come along to the next meeting in the fall.

BOOK REVIEWS

JACQUELINE DU PRÉ

One of my favorite recordings is the Elgar Cello Concerto in E Minor, Opus 85, played by Jacqueline du Pré (EMI London Symphony Orchestra, conducted by Sir John Barbirolli, 1965. CD remastering 1986). For some years, I would often put it on late at night, after work was done, and let it play as I settled for sleep. It is a classic recording of "the quintessential English work with which the quintessentially English girl would be linked for life." Tragically, the talented life of this magical young woman would be very short.

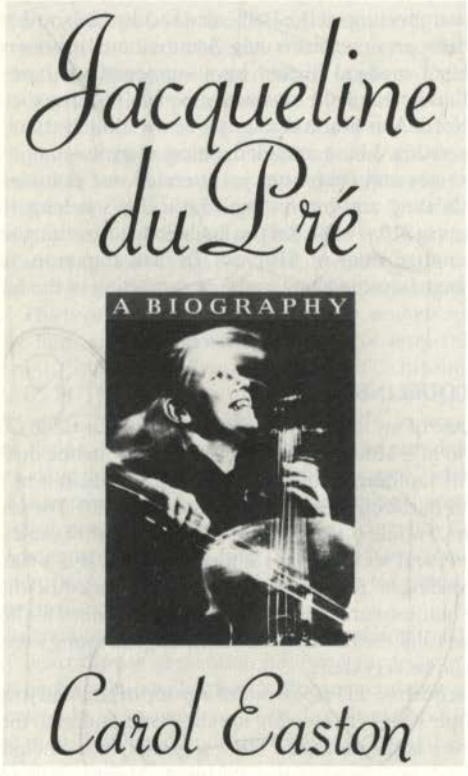
Jacqueline du Pré was one of a group of talented young people who were crossing the stages of London to thundering applause in the 60s – a group which included Ashkenazy, Barenboim, Perlman, Mehta, Williams, Zukerman. We were living in London at the time and I remember we wanted to hear all the concerts, but with little money and four children under six, we had to at

EDITOR'S NOTE

Dr. Murray in his new position as Professor of Medical Humanities, Dalhousie Medical School will provide this column on a regular bases. We welcome his broad based insight.

least show some restraint in our ticket purchase. I recognized I could hear Ashkenazy at the piano over a lifetime, so would attend seniors like the octogenarian Rubenstein. We said Rubenstein was now in his 80s so this may be his last concert. Ten years later we were again living in London and Rubenstein was billed at Royal Festival Hall the week we arrived.

A recent biography of Jacqueline: *Jacqueline du Pré: A Biography*. By Carol Easton, Toronto: Summit Books, 1989, outlines her early life as a passionate, committed cellist who had few friends and talked in lonely moments to her cello. She was recognized early as a great talent and by age 17 was receiving rave notices internationally. Although the wonderful recording of the Elgar Concerto I have is 1965, she had some warnings of unusual neurological symptoms as early as 1963. By 1973 her career, and that of her talented husband, Daniel Barenboim, was meteroric, but she was beginning to go on stage with numbness in her hands, heaviness in her arms and terror in her heart, as she didn't know what sounds she would make or how she would find the notes. Recognized as one of the great talents of the musical world, reviewers were puzzled and disappointed by her playing. Shortly afterwards she was diagnosed as suffering from multiple sclerosis.



Easton outlines briefly, and somewhat cooly, her rapid decline and unhappy life thereafter. Actually her life before was not "normal" but her pushy mother, disjointed schooling and lonely growing years were always in the background as long as she could play her cello. When she first played the Elgar Concerto she said she was not nervous but excited, and this awkward teenager, awkward only when not playing her 1673 Stradivarius, said she walked on to the stage feeling she was in front of a crowd of friends who came to hear her play, and was moved by that thought. With this feeling in her soul she sat in front of the orchestra, nestled the Strad between her knees and began to play. The music brought tears to many at the time, and the recording still has that capacity.

When we returned to London on sabbatical in 1985, Jacqueline was living around the corner from our apartment at Notting Hill Gate, alone except for a stern nurse. She developed pneumonia and slipped into a coma in October 1987. Some friends at her bedside, thinking someone in coma might be able to hear, played a recording of the Schuman Cello Concerto, which she loved, and while it was playing she died.

When you read Easton's account of her life, the failing marriage as one of the meteoric duo falters,the friends who wander away, the parents who seldom visit because they can't forgive her for becoming Jewish to marry Barenboim, the cold nurses who are her only constant companions, you hear more depth and more pathos in the evocative moods of the Elgar Concerto.

Although I feel a great sadness when I think of this young woman with progressive MS while listening to her music, I think she should be remembered for the wonder of this recording, and the picture of her playing her beloved cello, her head flung back, long hair flying, and an ecstatic smile on her face.

Easton was a friend who continued to visit during the last year's of du Pré's life. The book doesn't capture the magic, but fills in some of the spaces for those of us who knew part of the story and loved the music.

BRIEF REVIEWS

The *Medical Humanities Review*, a semiannual publication of the Institute for the Medical Humanities, University of Texas at Galveston, is an excellent journal devoted to all aspects of the medical humanities. The most recent issue had 17 papers on history, ethics, social and political questions and book reviews. A great read. Institute for the Medical Humanities, The University of Texas Medical Branch, Galveston, Texas, USA, 77555-1311. ($20. US).

Tomorrow's Doctors: The Path to Successful Practice in the 1990s. by Benjamin H. Natelson M.D. A Professor of Neurosciences at the New Jersey School, of Medicine, this book outlines for prospective medical students and students the changing pattern of medicine and the challenges for young physicians. He differentiates between the idea of a physician as a "body plumber", and the doctor who is a caregiver and educator to patients. Very clearly and sensitively written, and shows the aspiring physician the importance of the scientifically trained humanistic caregiver of the future. (Insight Books. New York: Plenum Press, 1990. $19.95.

Dead Certainties by Simon Schama. (Toronto: Alfred A Knoff, 1991. $26.00). This was a Christmas gift from Dr. Karen Mann, and a most unusual book. I was first captivated by it's beautiful appearance, with a tiny still life with skull, set on a matte black cover. Not judging a book by it's cover, I was then puzzled by the format and had to reread the introduction to note that he is telling two separate stories, each told from a series of perspectives. One story is the death of General Wolfe, and the other of the murder and dismemberment of Dr. Parkman of Harvard Medical School. Each is a reconstructed history (he subtitles his book "Unwarranted Speculations"), through the eyes of different people and different times. Thus you see the event as Schama feels it would have been seen, and he gives the stories a ring of authenticity and depth that capture your interest. The most riviting is the growing puzzle of the disappearance of Dr. Parkmann, his reappearance in pieces at Harvard Medical College, and the trial of a Professor of Chemistry for the crime. We see the event through the eyes of the Professor, the lawyer, and the janitor who found the remains. Pack this one for your next trip or weekend away.

MY BEDSIDE READING LIST

As an eclectic reader, I buy lots of new and many more older and old books. I have no pressure to always read the new books, although I quickly turn to the book reviews in the journals, and prefer the *New York Times Book Reviews* to the newspapers with my morning coffee. My reading list in each issue will thus have new and older and old books, whatever I find of interest and think you might find of interest. The most interesting of them will be reviewed more fully in later issues of the *Journal.*

Philosophy and Medical Welfare. Editors J.M. Bell and Susan Mendus. New York: Cambridge University Press, 1988.

Life Itself: A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life. By Dr. Robert Rosen. New York: Columbia University Press, 1991. (Dr. Rosen is Professor of Physiology and Biophysics at Dalhousie Medical School).

Intoxicated by My Illness: and Other Writings on Life and Death. By Anatole Broyard. New York: Clarkson Potter Publishers, 1992.

Letters to His Parents: 1839-1864. By Rudolf Virchow. Edited by Marie Virchow Rabl. 1989.

The Private Life of Dr. Watson. By Michael Hardwick. New York: E.P. Dutton Inc., 1983. □

ROUTINE SWAN-GANZ CATHETERIZATION IN AORTIC SURGERY

Continued from page 17.

5. Pierson MG and Funk M. Technology Versus Clinical Evaluation for Fluid Management Decisions in CABG Patients. *Image* 1989; **21**:192-195.
6. Tuman KJ, McCarthy RJ, Spiess BD, *et al.* Effect of Pulmonary Artery Catheterization on Outcome in Patients Undergoing Coronary Artery Surgery. *Anesthesiology* 1989; **70**:199-206.
7. Vella V, Duthie G, Shandad A and Shute K. Aortic Aneurysms – Who Should Do Them? *Ann R Coll Surg Engl* 1990; **72**:215-217.
8. Veith F, Goldsmith J, Leather RP, Hannan E. The Need for Quality Assurance in Vascular Surgery. *J Vasc Surg* 1991; **13**:523-526.
9. Pairolero PC. Repair of Abdominal Aortic Aneurysms in High-Risk Patients. *Surg Clin North Am* 1989; **69**:755-768.

LITHIUM AUGMENTATION IN SCHIZOAFFECTIVE DEPRESSION

Continued from page 20.

16. Sulser F. Serotonin-Norepinephrine receptor interactions in the brain: Implications for the pharmacology and patho-physiology of affective disorders. *J Clin Psychiat* 1987; **48**: (3 suppl) 12-18.
17 Sulser F., Update on neuroreceptor mechanisms and their implications for the pharmacotherapy of affective disorders. *J Clin Psychiat* 1986; **47**: (10 suppl) 13-18.
18 Manier DH, Gillespie DD, Steranka LR, *et al.* A pivotal role for serotonin in the down regulation of Beta adrenoceptores by antidepressants. *Experientia* 1984; **40**: 1223-1226.
19 Wood AJ, Goodman GM. A review of the biochemical and neuropharmacological actions of lithium. *Psychol Med* 1987; **17**: 579-600.

Appreciations

DR. BENJAMIN ROY MAXWELL

1909-1992

After nine months of failing health, Roy Maxwell, Radiologist at the Glace Bay General Hospital died peacefully in the hospital where he served as a Radiologist for close to half a century.

He was born in Dominion C.B. in 1909. While he was a young child he and his family moved to Glace Bay. He attended schools there and graduated from Glace Bay High School. Following his high school graduation he entered Dalhousie University for pre-medical studies. Following this he went to McGill University where he completed his medical studies, graduating in 1937. He returned to his native town and entered into practice of medicine with the late Dr. W.W. Patten. He later joined the general practice of the late Drs. Calder and McAskill, where he continued to practise until the early forties. Radiology was his chosen specialty.

For this specialty, he took his training in Chicago and in the Halifax Infirmary in Nova Scotia. Successfully completing his studies he received his FRCP(C).

He practised Radiology in Halifax for a short time until he returned to Glace Bay where he served at the Glace Bay General Hospital until 1991. For several years he served as a part time radiologist at the New Waterford General and later Consolidated Hospital, and also at the St. Joseph's Hospital later the Glace Bay Community Hospital in Glace Bay.

He was an avid sportsman, in his younger years. As a pitcher, for the Dominion Hawks baseball team, his abilities were recognized by his team, opponents and fans. He was one of the best.

He married Kathleen Calder in 1942. She was the only daughter of the late Dr. Allister and Mabel Calder. He lived to celebrate their fiftieth year of marriage this year. They had two children, Allister who resides in Dominion, C.B. and Beverly who resides in Mira and three grandchildren.

Roy was a gentle, quiet and good humored man, who besides his work in medicine always gave priority to his wife, children and grandchildren. He loved his home and his second home – his cottage on the Mira.

A good man, a quiet leader, he endeared himself to his staff, patients and medical colleagues who with his wife and family share in the loss of this fine person.

Edgar Linton's words are most appropriate to Roy.

"The brightest and most enduring flowers along the waysides of life are smiles, the sparkle of the eye, loving words, little acts of kindness . . . they never wholly fade from memory. Often after years they are brighter than on the day we beheld them".

Dr. William M. Nicholson
Reserve Mines, Cape Breton, N.S.

DR. JOHN D. MILLER

Dr. John D. Miller (42) of Newport Beach, California, died November 25, 1992. Born in Fall River, Halifax County, he received his medical degree from Dalhousie University in 1975 and went on to do a residency in Pediatrics at McGill University and Universite de Montreal.

He furthered his studies with fellowships in Pediatric Endocrinology at Montreal Children's Hospital and the Children's Hospital Medical Center at the University of Cincinnati, Ohio.

He authored and co-authored many articles and papers in the field of endocrinology disorders in children.

A member of both Canadian and American Medical Societies, Dr. Miller was the recipient of many awards and honours including the Queen Elizabeth II Scientist Award from the Medical Research Council of Canada, the Ontario Ministry of Health Career Scientist Award, and a two-time recipient of the Outstanding Full-Time Faculty Award from the University of California, Irvine.

At the time of his death, Dr. Miller was the Director of Pediatric Diabetes at the University of California, Irvine.

He is survived by his father David, sister Lois and brother Ross.

Mr. Ross Miller
Halifax, N.S.

DR. MARY JANE SULLIVAN

Physician, Mother and Friend

Mary Jane Sullivan was born in St. John, New Brunswick and obtained her undergraduate degree from Dalhousie University in Halifax. She enroled at Memorial University's Faculty of Medicine in 1975, obtaining her Doctorate of Medicine in 1979. She later interned at Dalhousie.

Mary Jane returned to Newfoundland in 1980 and served as Casualty Officer at Carbonear General Hospital and St. Clare's Mercy Hospital. For the next several years, she worked as general practitioner on staff at the Waterford Hospital.

It was during her residency training that Mary Jane and her husband Wilfred Wareham, well-known Newfoundland folklorist and traditional singer, became the parents of two beautiful daughters, Bridget and Angela. In 1988, she accepted a position as Staff Psychiatrist at Bridgewater Hospital in Nova Scotia. Her third daughter, Lindsay, was born in 1990.

Earlier this year, Mary Jane was diagnosed with leukemia, and on September 16th, after a courageous battle, she died at Victoria General in Halifax. It is Mary Jane's wish that in lieu of flowers, donations may be made to a memorial trust fund established for her three daughters by her medical school classmates.

Donations to the **Mary Jane Sullivan Memorial Fund** can be sent c/o Dr. Bruce Short, 217 Waterford Bridge Road, St. John's, Newfoundland A1E 1E4, or deposited at the CIBC Branch located in Churchill Square, St. John's.

Your remembrance of Mary Jane in this manner is greatly appreciated.

Sheila Lynch, MD, FRCPC
Reprinted from the NMA Communiqué
November 1992 □

ADVERTISERS' INDEX

OBITUARIES

Dr. John D. Miller, (42) of Newport Beach, California, died on November 25, 1992. Born in Fall River, Nova Scotia he received his medical degree from Dalhousie Medical School and then continued further studies in paediatrics and endocrinology in Montreal and Cincinnati, Ohio. He authored and co-authored many writings in the field of endocrine disorders of children and was Director of Paediatric Diabetes at the University of California. He was a member of The Medical Society of Nova Scotia. He is survived by his father, a brother and a sister. The *Journal* extends sincere sympathy to his family.

Dr. Otto H. Horrelt, (59) of Halifax, Nova Scotia died on December 21, 1992. Born in Dalhousie, New Brunswick he received his medical degree from Dalhousie Medical School in 1960. He continued his studies in anaesthesia and practised at the Victoria General Hospital for 15 years. He was a member of The Medical Society of Nova Scotia and the Canadian Medical Association. He is survived by his three sons, to whom the *Journal* extends sincere sympathy.

"Both birth and death are great mysteries. If death is not a prelude to another life, the intermediate period is a cruel mockery."

Mohandas K. Gandhi (1869-1948)

Pr BECLOVENT® INHALER
Pr BECLOVENT® ROTACAPS®
Pr BECLODISK® DISKHALER®
Pr BECLOFORTE® INHALER
Beclomethasone Dipropionate
Asthma Prophylaxis

Indications and Clinical Use – a) Treatment of steroid responsive bronchial asthma in patients not previously on steroids. b) Replacement or reduction of systemic steroids in steroid dependent patients.

Contraindications – Active or quiescent untreated tuberculosis; untreated fungal, bacterial and viral infections; primary treatment of status asthmaticus; moderate to severe bronchiectasis; hypersensitivity to any ingredients of preparation.

Warnings – Particular care needed in patients transferred from systemic steroids to beclomethasone dipropionate. Deaths due to adrenal insufficiency have occurred during and after transfer. If adrenal insufficiency is suspected, resume systemic steroids. Recovery of hypothalmic-pituitary-adrenal (HPA) function after systemic steroid withdrawal requires a number of months, during which time patients may exhibit signs of adrenal insufficiency after trauma, surgery, or infection (particularly gastroenteritis). Beclomethasone dipropionate may control asthmatic symptoms but systemic steroids will be required in such emergencies.

Beclomethasone dipropionate is not to be regarded as a bronchodilator and is not intended for rapid relief of bronchospasm.

During periods of stress or severe asthmatic attack after transfer from systemic steroids, patient should be instructed to resume systemic steroids in large doses, contact physician immediately for further instructions and carry warning card indicating need for systemic steroids in such eventualities. Periodic routine tests of adrenal cortical function, including measurement of early morning and evening cortisol levels should be performed to assess risk of adrenal insufficiency.

Pharyngeal and laryngeal candidiasis is cause of concern because extent of penetration into respiratory tract is unknown. May require appropriate antifungal treatment and/or discontinuation of treatment if severe.

Transfer to beclomethasone dipropionate may unmask allergic conditions (eg. rhinitis, conjunctivitis, eczema) previously controlled by systemic steroid.

Patients should be instructed to contact their physician immediately when episodes of asthma not responsive to bronchodilator treatment occur during the course of treatment with beclomethasone dipropionate.

Transfer Procedure – When patients previously treated with systemic corticosteroids for prolonged periods are transferred to beclomethasone dipropionate, inhaled and systemic steroid should be given concomitantly initially, with gradual decrease of dose of the latter. A slow rate of withdrawal cannot be overemphasized. In adults, the usual rate of withdrawal of the systemic corticoid is the equivalent of 1.0 mg of the daily dose of prednisone at no less than weekly intervals if the patient is under close supervision. In children, the rate of withdrawal is 1.0 mg of the daily dose of prednisone every eight days. If continuous supervision is not feasible, the withdrawal of the systemic steroid should be slower, approximately 1.0 mg of prednisone (or equivalent) every ten and every twenty days in adults and in children, respectively. If withdrawal symptoms occur (eg. joint pain and/or muscular pain, lassitude, depression) resume previous dose of systemic steroid for one week before further decrease attempted. Under stressful conditions or severe exacerbation of asthma after complete withdrawal of systemic steroid, resume use of latter to avoid adrenal insufficiency. Some patients cannot discontinue systemic steroids completely and require minimal dose in addition to beclomethasone dipropionate.

Precautions – Pulmonary infiltrates with eosinophilia may occur. Use of beclomethasone dipropionate in pregnancy and in nursing mothers of child-bearing age requires that possible benefits be weighed against potential hazards to mother, embryo or fetus. It is not known whether beclomethasone dipropionate would be secreted in human milk, but it is suspected to be likely. Infants of mothers who received substantial doses of corticosteroids during pregnancy should be observed carefully for hypoadrenalism. Glucocorticoids are known teratogens in rodent species and beclomethasone dipropionate is no exception. Corticosteroids may mask some signs of infection and new infections may appear. During long-term therapy, assess pituitary-adrenal function and hematological status periodically. Effect of corticosteroids enhanced in patients with hypothyroidism and cirrhosis. Use ASA cautiously with corticosteroids in hypoprothrombinemia. Advise patients to inform subsequent physicians about prior use of corticosteroids. To ensure the proper dosage and administration of the drug, the patient must be instructed by a physician or other health professional in the use of the inhaler.

Beclovent/Becloforte Inhalers: Fluorocarbon propellants may be hazardous if they are deliberately abused.

Adverse Reactions – No significant adrenal cortical suppression observed when beclomethasone dipropionate daily dose 1000 mcg or less. Above 1000 mcg reduction of plasma cortisol may occur indicating possible adrenal cortical suppression.

Rare cases of immediate and delayed hypersensitivity reactions, including urticaria, angioedema, rash, and bronchospasm have been reported after the use of beclomethasone dipropionate.

Candida albicans in mouth and throat frequently occur with therapeutic dosage. Clinically apparent in 0 to 43% (average 15%) of cases. Incidence of oropharyngeal candidiasis in children lower than in adults. Incidence of candidiasis can generally be held to minimum by having patient rinse mouth with water after each inhalation.

Overgrowth of Aspergillus niger in conjunction with Candida albicans found in some studies. A few patients have complained of hoarseness, dry mouth or throat irritation.

Overdose – Chronic overdose may cause systemic steroid effects, eg. adrenal suppression, hypercorticism. Decreasing dose will abolish these side effects.

Dosage and Administration –
Adults – Maximum daily dose not to exceed 1000 mcg.

Usual dose:

Beclovent Inhaler – Two inhalations (100 mcg) 3 to 4 times daily. Becloforte Inhaler – One inhalation (250 mcg) 2 to 4 times daily. Some patients may do well with two inhalations (500 mcg) twice daily. Note: Becloforte Inhaler to be used only when total daily dosage of beclomethasone dipropionate required is 500-1000 mcg. Beclovent Rotacaps – One 200 mcg Rotacap 3 to 4 times daily. Beclodisk – 200 mcg 3 to 4 times daily. Note: As maintenance, many do well on two 100 mcg inhalations daily.

Adolescents – Above 14 years, adult dose (above 16 years for Becloforte).

Children – 6 to 14 years – Maximum daily dose not to exceed 500 mcg/day.

Beclovent Inhaler – Two inhalations (2 × 50 mcg), 2 to 3 times daily. May be increased to 4 times. Beclovent Rotacaps – One 100 mcg Rotacap 2 to 3 times daily. Becloforte Inhaler – Not recommended for children under 16. Beclodisk – One 100 mcg blister 2 to 4 times daily.

Children – 3 to 5 years. Insufficient experience with Rotacaps and Beclodisk in children under 6 years. Beclovent Inhaler – One inhalation (50 mcg) twice daily. May be increased to 3 times.

Supplied

Beclovent Inhaler – Metered dose aerosol delivering 50 mcg beclomethasone dipropionate with each depression of valve. 80 and 200 dose containers.

Becloforte Inhaler – Metered dose aerosol delivering 250 mcg beclomethasone dipropionate with each depression of valve. In aluminum canister fitted with metering valve. Each unit housed in actuator/adaptor. 80 and 200 dose containers.

CAUTION: Container may explode if heated. Store below 30°C. Protect from frost and direct sunlight.

Beclovent Rotacaps – Each Rotacap contains: 100 mcg or 200 mcg microfine beclomethasone dipropionate and larger particle lactose in buff or brown coloured gelatin capsules respectively. Screwcap containers of 100.

Contents of Rotacap inhaled using Rotahaler separates capsules into halves and releases drug by breath actuation when patient inhales.

Beclodisk Diskhaler – Beclodisk blisters contain mixture of microfine beclomethasone dipropionate in double foil blister pack. Each blister contains 100 mcg or 200 mcg beclomethasone dipropionate on buff or brown coloured disks respectively containing 8 blister packs.

Intended for use only in Beclodisk Diskhaler. Contents of blister deposited in Diskhaler when blister pierced with Diskhaler needle immediately prior to use. Contents inhaled by breath actuation. Diskhaler available separately. Beclodisk Disks 100 mcg and 200 mcg supplied in cartons of 15.

REFERENCES: 1. Karalus NC, and Harrison AC, Inhaled high-dose beclomethasone in chronic asthma. *NZ Med J* 1987; 100 (824): 305-308. **2.** Brogden RN, Heel RC, Speight TM, Avery GS. Beclomethasone dipropionate. A reappraisal of its pharmacodynamic properties and therapeutic efficacy after a decade of use in asthma and rhinitis. *Drugs*, 1984, 28: 99-126. **3.** Broder I, Tarlo SM et al. Safety & efficacy of long-term treatment with inhaled beclomethasone dipropionate in steroid-dependent asthma. *Can Med Assoc J*, 1987, 136; 2: 129-135. **4.** Dutoit JI, Salome CM et al. Inhaled corticosteroids reduce the severity of bronchial hyperresponsiveness in asthma but oral theophylline does not. *Am Rev Resp Dis*, 1987, 136: 1174-1178. **5.** Becloforte Dosage Profile, Glaxo Canada from COTI, 1991, IMS Canada. Data on file, Glaxo Canada Inc.

Product monograph available to Physicians and Pharmacists upon request.

beclomethasone dipropionate
"BECLOVENT®
beclomethasone dipropionate
"BECLODISK®
PAAB CCPP
beclomethasone dipropionate
Glaxo Glaxo Canada Inc. "BECLOFORTE®

Atrovent®

(ipratropium bromide)

INHALATION SOLUTION 250 µg/mL

THERAPEUTIC CLASSIFICATION

Bronchodilator

INDICATIONS AND CLINICAL USES

Atrovent (ipratropium bromide) solution is indicated for the therapy of acute exacerbations of chronic bronchitis. Atrovent solution, when used in conjunction with a β_2-adrenergic stimulant solution such as fenoterol or salbutamol, is indicated for acute asthmatic attacks. It is to be administered by compressed air or oxygen driven nebulizers.

CONTRAINDICATIONS

Known hypersensitivity to Atrovent (ipratropium bromide), to any of the product ingredients, or to atropinics.

WARNINGS

Atrovent (ipratropium bromide) solution in the 20 mL multidose bottle contains preservatives (benzalkonium chloride and disodium ethylene diamine tetraacetic acid - EDTA-disodium). It has been reported that these preservatives may cause bronchoconstriction in some patients with hyperreactive airways.

The 2 mL unit dose vial does not contain preservatives.

Atrovent should not be used alone for the abatement of an acute asthmatic attack since the drug has a slower onset of effect than that of an adrenergic β_2 agonist.

Care should be taken to ensure that the nebulizer mask fits the patient's face properly and that nebulized solution does not escape into the eyes. There have been isolated reports of ocular complications (i.e., mydriasis, increased intraocular pressure, angle closure glaucoma) when nebulized ipratropium bromide either alone or in combination with an adrenergic β_2 agonist solution has escaped into the eyes. In the event that glaucoma is precipitated or worsened, treatment should include standard measures for this condition.

PRECAUTIONS

General:

-Patients should be instructed in the proper use of the nebulizer.

-Caution is advised against accidental release of the solution into the eyes.

-In patients with glaucoma, prostatic hypertrophy or urinary retention, Atrovent (ipratropium bromide) should be used with caution.

-If a reduced response to Atrovent becomes apparent, the patient should seek medical advice.

-Atrovent solution, when administered to patients with acute severe asthma, should be used with concomitant β_2-adrenergic stimulant therapy.

Use in Pregnancy:

The safety of Atrovent in pregnancy has not been established. The benefits of using Atrovent when pregnancy is confirmed or suspected must be weighed against possible hazards to the fetus. Studies in rats, mice and rabbits showed no embryotoxic nor teratogenic effects.

Use During Lactation:

No specific studies have been conducted on excretion of this drug in breast milk. Benefits of Atrovent use during lactation should therefore be weighed against the possible effects on the infant.

Use in Children:

The efficacy and safety of Atrovent in children younger than 5 years has not been established.

Use with Other Drugs:

In patients receiving other anticholinergic drugs, Atrovent should be used with caution because of possible additive effects.

In patients with glaucoma or narrow anterior chambers, the administration by nebulizer of combined Atrovent-β_2 agonist solution should be avoided unless measures (e.g., use of swimming goggles) are taken to ensure that nebulized solution does not reach the eye. Exposure of the eyes of such patients to a nebulized combination of Atrovent and a β_2 agonist solution has been reported to result in increased intraocular pressure and/or acute angle closure.

Atrovent solution with preservatives (i.e. from the 20 mL multidose bottle) should not be mixed with sodium cromoglycate, as this produces a cloudy solution caused by complexation between the preservatives and sodium cromoglycate. If the patient's condition requires the administration of sodium cromoglycate, it should be given in combination with Atrovent solution without preservatives (i.e., from the unit dose vial).

ADVERSE REACTIONS

The frequency of adverse reactions recorded in 214 patients receiving Atrovent (ipratropium bromide) solution was as follows, given by percentage of patients reporting: Dry mouth or throat, 9.3; Bad taste, 5.1; Tremor, 4.2; Exacerbation of symptoms, 4.2; Burning eyes, 0.9; Nausea, 0.9; Sweating, 0.9; Cough, 0.9; Headache, 0.5; Palpatations, 0.5.

The adverse effect judged to be most severe was exacerbation of symptoms. This occurred in 8 patients treated with Atrovent solution alone, 6 of whom withdrew from the clinical studies.

Bronchospasm occurred in 3 patients with acute severe asthma who received Atrovent solution alone. In two patients, this was reversed after therapy with β_2 sympathomimetic solution. The third patient received no other therapy.

The following table compares the incidence of adverse effects of the combination of Atrovent and a β_2 agonist (either fenoterol or salbutamol) solution with that of the β_2 agonist alone.

ADVERSE EFFECT	ATROVENT + β_2 AGONIST (% of 94 patients)	β_2 AGONIST (% of 96 patients)
Tremor	31.9	26.0
Dry mouth	16.0	28.1
Bad taste	16.0	13.5
Vomiting	2.1	2.1
Palpitations	2.1	1.0
Headache	1.1	2.1
Cough	1.1	0.0
Flushing	1.1	0.0
Dizziness	0.0	1.0
Numbness in leg	0.0	1.0

There have been isolated reports of ocular effects such as mydriasis, increased intraocular pressure, and acute glaucoma associated with the escape of nebulized ipratropium bromide-alone or in combination with a β_2 agonist solution into the eyes.

DOSAGE AND ADMINISTRATION

In adults, the average single dose is 1-2 mL of Atrovent (ipratropium bromide) solution, containing 250-500 µg of ipratropium. In children, aged 5-12 years, the recommended dose is 0.5-1 mL (125-250 µg of ipratropium). This should be diluted to 3-5 mL with preservative free sterile Normal Saline [Sodium Chloride Inhalation Solution, USP 0.9%] or with a bacteriostatic sodium chloride solution, 0.9% preserved with benzalkonium chloride (see PHARMACEUTICAL INFORMATION).

Nebulization should take place using a gas flow (oxygen or compressed air) of 6-10 L/minutes and the solution nebulized over a 10-15 minute period. The Hudson Updraft™, Bennett Twin Jet® and Inspiron Mini-Neb® nebulizers, with facemask or mouthpiece have been used. The manufacturers' instructions concerning cleaning and maintenance of the nebulizer should be strictly followed.

Treatment with Atrovent solution may be repeated every 4-6 hours as necessary.

PHARMACEUTICAL INFORMATION

Stability and Storage Recommendation:

20 mL Bottle: Unopened bottles of Atrovent (ipratropium bromide) solution should be stored at controlled room temperature (below 30°C).Solutions diluted with preservative free sterile Sodium Chloride Inhalation Solution, USP 0.9% should be used within 24 hours from time of dilution when stored at room temperature and within 48 hours when stored in the refrigerator.

Dilutions may also be made with a bacteriostatic sodium chloride solution 0.9% which contains benzalkonium chloride as the bacteriostatic agent (see WARNINGS). This diluted solution may be stored at room temperature and used within 7 days.

Controlled laboratory experiments using mixtures of Atrovent solution with Alupent® (orciprenaline sulfate), Berotec® (fenoterol hydrobromide) or salbutamol sulfate (6mg/mL preserved with benzalkonium chloride) solutions and diluted with a sterile bacteriostatic sodium chloride solution 0.9% (i.e. normal saline), preserved with benzalkonium chloride, indicated that such mixtures were stable for 7 days at room temperature. For the preparation of such mixtures, it is recommended that only sterile solutions of bacteriostatic sodium chloride 0.9% preserved with 0.01% benzalkonium chloride be used to maintain the level of preservative in the mixture.

The safety of preservatives other than benzalkonium chloride has not been established.

Incompatibilities: Atrovent solution with preservatives (i.e. from the 20 mL multidose bottle) should not be mixed with sodium cromoglygate solution, as this produces a cloudy solution caused by complexation between the preservatives and sodium cromoglycate. If the patient's condition requires the administration of sodium cromoglycate, it should be given in combination with Atrovent solution without preservatives (i.e., from the unit dose vial).

2 mL Unit Dose Vial: Unopened unit dose vials of Atrovent solution should be stored at controlled room temperature (below 30°C) and protected from light. If required, the solution should be diluted with a preservative free sterile sodium chloride solution 0.9% and used immediately. Any solution remaining in the vial must be discarded.

The solution is physically compatible with Alupent® (orciprenaline sulfate), Berotec® (fenoterol hydrobromide) or salbutamol sulfate (6 mg/mL) solutions. If such mixtures are prepared, they should be diluted with preservative free sterile sodium chloride solution 0.9% and used immediately. Any unused portion of such combined solutions must be discarded.

AVAILABILITY

20 mL Bottle: Atrovent (ipratropium bromide) solution is provided as 20 mL clear, colourless or almost colourless solution containing 250 µg/mL (0.025%) Atrovent in isotonic solution. This solution is preserved with benzalkonium chloride 250 µg/mL and EDTA-disodium 500 µg/mL at pH 3.4 in an amber glass bottle with screwcap.

2 mL Unit Dose Vial: Atrovent solution is also provided as 2mL of clear, colourless solution containing 250 µg/mL (0.025%) ipratropium bromide in isotonic solution, presented in a plastic single use vial. One vial contains a total of 500 µg of ipratropium bromide.

The complete Product Monograph for Atrovent (ipratropium bromide) Inhalation Solution is available to health professionals on request. Patient Information/ Instructions are provided with the solution.

REFERENCES:

1. Rebuck AS, Chapman KR, Abboud R, *et al.* Nebulized anticholinergic and sympathomimetic treatment of asthma and chronic obstructive airways disease in the emergency room. *Amer J Med* 1987;82:59-64. 2. Product Monograph - Atrovent (ipratropium bromide) Inhalation Solution (rev. Nov. 18, 1991). 3. Beck R, Robertson C, Galdes-Sebaldt M, Levison H. Combined salbutamol and ipratropium bromide by inhalation in the treatment of severe acute asthma. *J Ped* 1985;107(4):605-608. 4. Watson WTA, Becker AB, Simons FER. Comparison of ipratropium solution, fenoterol solution, and their combination administered by nebulizer and face mask to children with acute asthma. *JAllergy Clin Immunol* 1988;82:1012-1018. 5. Reisman J, Galdes-Sebaldt M, Kazim F, Canny G, Levison H. Frequent administration by inhalation of salbutamol and ipratropium bromide in the initial management of severe acute asthma in children. *J Allergy Clin Immunol* 1988;81:16-20. 6. Chan CS, Brown IG, Kelly CA, Dent AG, Zimmerman PV. Bronchodilator responses to nebulized ipratropium and salbutamol singly and in combination in chronic bronchitis. *Br J Clin Pharmac* 1984;17:103-105.

Boehringer Ingelheim

Dedicated to Respiratory Care

PAAB CCPP

Boehringer Ingelheim (Canada) Ltd./Ltée
5180 South Service Rd., Burlington, Ontario L7L 5H4

B-020/92

THE MEDICAL SOCIETY OF NOVA SCOTIA

NOVA SCOTIA DIVISION OF THE CANADIAN MEDICAL ASSOCIATION

MEMBERS OF EXECUTIVE COMMITTEE

OFFICERS

President ..... J.R. LeMoine
President-Elect ..... R.R. Kimball
Past President (Immediate) ..... R. Stokes
Chairman of the Executive Committee ..... K.R. Crawford
Vice-Chairman ..... R.O. Holness
Treasurer ..... K.R. Langille
Honorary Secretary ..... Anne Houston
Member-At-Large .....

OBSERVERS AND STAFF

Economics Committee Chairman ..... L.P.M. Heffernan
Executive Director ..... R.J. Dyke
Director, Health Policy & Economics ..... Paul Childs
Associate Director, Health Policy &Economics ..... M.K. Needler
Director of Communications & Public Affairs ... Dorothy Grant
Manager, Corporate Affairs ..... Shirley Miller

BRANCH SOCIETY REPRESENTATIVES

Antigonish-Guysborough ..... J.D. Chiasson
Bedford-Sackville ..... C.M. Childs
Cape Breton ..... D. P. Hickey
Colchester-East Hants ..... F.J. Carpenter
Cumberland ..... T.J.G. Mullan
Dartmouth ..... M. Ellis, D.J. Chevrie
Eastern Shore ..... M. MacQuarrie
Halifax ..... J.A. McLean, B.L. Reid
Inverness-Victoria ..... J.C. Aucoin
Lunenburg-Queens ..... R. Côté
Pictou ..... H.P. MacDonald
Shelburne ..... P. Robbins
Sydney ..... J.E. Sampson
Valley ..... A.R. Ahmad, K. Buchholz
Western ..... I. Brodarec
Student Members ..... Sonia Verma, Steve Miller, Tina Dempsey
PARI-MP Representatives ..... Arun Mathur, Kevork Peltekian

OBSERVERS

Editor-in-Chief – The Nova Scotia Medical Journal ..... J.F. O'Connor
C.M.A. Board of Directors ..... Rob Stokes
C.M.A. Council on Health Care ..... B.N. Chutskoff
C.M.A. Council on Health Policy and Economics ..... R.J. Gibson
C.M.A. Council on Medical Education ..... G.P. Ernest
M.D. Advisory Committee ..... E.V. Rafuse

STANDING COMMITTEES

	Chairman
Archives	E.G. Nurse
By-Laws	P.W. Littlejohn
Child Health	N.P. Kenny
Communications	V.P. Audain
Community Health	M.J. Cussen
Environment	G.H. Bethune
Ethics	D.F. Fay
Gynecological Cancer (Screening Program)	R.C. Fraser
Home Care	M. Kazimirski
Hospital & Emergency Services	D.M. Maxwell
Liaison Committees:	President
(i) Minister of Health	
(ii) Workers' Compensation Board	
(iii) Registered Nurses' Association	
(iv) Faculty of Medicine	
Maternal & Perinatal Health	A.C. Allen
Mediation	President
Medical Education	
Membership Services	
Morality Review (Appointed by and Reports Through Section of Anaesthesia)	A.C. Walker
Occupational Health	
Pharmacy	S.G. Carruthers
Professionals' Support Program	D. Eisner, DDS
Risk Management	J.P. Anderson
Senior Advisory Committee	W.D. Canham
Site Development	I.A. Cameron

BRANCH SOCIETIES

	President	Secretary
Antigonish-Guysborough	J. Hamilton	S. Rappard
Bedford-Sackville	J. Fitzgerald	J. Fraser
Cape Breton	B.J.M. O'Brien	P.W. Littlejohn
Colchester-East Hants	F.J. Carpenter	B.R. Wheeler
Cumberland	F. Bravo	S.I. Awan
Dartmouth	D.J. Cheverie	L. Hardy
Eastern Shore	D.P. Sinha	W.E. Chernin
Halifax	B.L. Reid	D.A. Stinson
Inverness-Victoria	N.G. Pillai	R.J. Genge
Lunenburg-Queens	B. Chutskoff	K.A. Barss
Pictou	P.T.C. Lee	A.B. Shaw
Shelburne	I.C. Cree	Mark Riley
Sydney	J.E. Sampson	Gail Bisson
Valley	J.D. Simms	R.C. Jung
Western	S.M.T. Leahey	R.P. Belliveau

SECTIONS

	President	Secretary
Anaesthesia	R. Shukla	D. Morrison
Emergency Medicine	J. Ross	G. Stewart
General Practice	P.W. Littlejohn	S.A. Canham
Internal Medicine	M. O'Reilly	K.R. Crawford
Internes & Residents	K. Pelekian	C. Zip
Obstetrics and Gynaecology	D.P. Kogon	J.B. Wenning
Ophthalmology	D.M. O'Brien	
Orthopaedic Surgery	E. Howatt	Wm. Stanish
Otolaryngology	C.C. Cron	
Paediatrics	J. Dooley	M. Vincer
Laboratory Medicine	B. Wright	A. Foyle
Psychiatry	A.E. Hipwell	S. Brooks
Radiology	M. Riding	D. Barnes
Surgery	G.A. Legere	J.P. Curry
Urology	J. Lawen	B.W. Palmer
Vascular Surgery	D.A. Pyne	R.S. Dunn

5 Spectacle Lake Drive
City of Lakes Business Park
Dartmouth, N.S B3B 1X7
(902) 468-1866 FAX 468-6578

THE NOVA SCOTIA MEDICAL JOURNAL

Published by

The Medical Society of Nova Scotia

GUIDELINES FOR AUTHORS

The entire manuscript should be typed double-spaced on one side only, with generous margins on all four sides. Tables should not be included in the text but typed on separate pages, as should the references and the legends for any figures and illustrations. Forward three copies of the manuscript.

Non-metric units should not be used in scientific contributions. Parts of the SI system are controversial or unfamiliar, especially concentrations of substances, gas tensions, blood pressure and radiological units, so that authors should provide conversion factors. Abbreviations should be defined when first mentioned and, if numerous, the author should provide a glossary which will be printed separately in a prominent place in the article.

In general, papers reporting on studies should adhere to the following sequence:

a) **Title page** – title of article (concise but informative); first name, middle initial and surname of each author, with academic degrees; names of department or institution to which the work should be attributed; name and address of author responsible for correspondence or reprints; source of support (if any).

b) **Summary or Abstract** – not over 150 words, summarizing the purpose, basic procedures, main findings and principal conclusions.

c) **Materials and Methods** – describe the selection of subjects, the techniques and equipment employed, the types of data collected, and the statistical tests used to analyze the data.

d) **Results** – describe in logical sequence, using tables and illustrations.

e) **Discussion** – emphasize new and important aspects, and the conclusions that follow from them. Recommendations, when appropriate, may be included.

f) **Acknowledgements** – only those persons who have made substantial contributions to the study.

g) **References** – usually limited to 10 for short papers and to a maximum of 20 for review articles. Number in sequence, in the order they are first mentioned in the text, with journal titles abbreviated as in *Index Medicus.*

Examples of the new format are:

1. Journal articles – list all authors when six or less (surnames followed by initials without periods); when seven or more, list only the first three and add *et al.*

Epstein SW, Manning CPR, Ashley MJ, Corey PN. Survey of the clinical use of pressurized aerosol inhalers. *Can Med Assoc J* 1979; **120**:813-816.

2. Book –

Fletcher C, Peto R. Tinker C, Speizer FE. *The Natural History of Chronic Bronchitis and Emphysema.* Oxford: Oxford University Press, 1976.

3. Chapter in book –

Deusche KW. Tuberculosis. In: Clark DW, MacMahon B, eds. *Preventive Medicine.* Boston: Little, Brown, 1967; pg 509-523.

h) **Tables** – type each on a separate sheet, number consecutively with *roman* numerals. Supply a brief title for each, give each column a short or abbreviated heading, and reserve explanatory material for footnotes.

i) **Figures and Illustrations** – professionally drawn and photographed, as glossy black and white prints, numbered consecutively with *arabic* numerals. List all legends on one page and state magnification of photomicrographs.

The senior author should accept responsibility by attaching a signed covering letter to the manuscript:

1. warranting that this manuscript has not been published previously and that none of this material is currently under consideration for publication elsewhere;
2. stating that the sources of all quotations have been cited and that, for extended quotations written consent has been obtained from the copywright owner(s); and
3. indicating the contribution made by each of the co-authors (for multi-author papers)

Mailing address:

Editor,
The Nova Scotia Medical Journal
5 Spectacle Lake Drive
City of Lakes Business Park
Dartmouth, N.S. B3B 1X7
Tel: (902) 468-1866
Fax: (902) 468-6578

When manuscript has been composed on a computer, a disk, which is an exact replica, should accompany the three printed copies. Please indicate the type of computer and software used.