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VOLUME 12 • ISSUE 1 • 2009

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ACKNOWLEDGMENTS

The following organizations, companies, and institutions deserve recognition for their generous contributions to the *McGill Journal of Medicine*.

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The entire MJM team would like to sincerely thank Dr. Phil Gold, our faculty advisor, and Dr. Richard I. Levin, Dean of Medicine, for their continued guidance, support and effort provided to the journal. We would also like to thank MedIt for their technical support and ongoing service.

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ISSN 1201-026X

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EDITORIAL

THE LOOMING ENVIRONMENTAL CRISIS

As governments around the world attempt to prop up our ailing economies by developing large stimulus packages in an attempt to restore and promote new growth and development, it appears that both health and environment have taken a back seat when in fact they should still be at the forefront of government policy. In this issue of the MJM we have assembled a collection of articles that discuss and investigate the close relationship that exists between health and environment, and we argue that as government officials attempt to restore our nation's economy, they should not overlook the important alliance that coexists between environment, the health of a nation's workforce and their GDP (1).

The policies of our predecessors have already left the world committed to many upcoming years of global warming, a predicament which will only be relieved by drafting and implementing critical policies in the coming years which aim to deter and prevent further climate change (2, 3). In fact, even modest increases in temperature have been associated with significant elevations in morbidity and mortality, especially in the most vulnerable members of society, the young and old (2, 4). Thus, as the Canadian population ages, with one in five expected to reach 65 years of age by 2026 (5), and as the lifespan of immunocompromised patients is prolonged thanks to the great feats of contemporary medicine, we must find a way to palliate the imminent increase in mortality in these most vulnerable groups due to the consequences of our deteriorating environment. For example, the World Health Organization estimated that there were at least 27,000 more deaths in Europe over the summer of 2003 relative to the previous years which was associated with unusually elevated temperatures recorded during the same time period (6). If such an alarming event could occur in a relatively well-endowed region of the globe, the repercussion of human-induced climate derangement on casualties in the third-world, although difficult to document, likely reaches pandemic proportions in an era where the scarcity of medical aid and adequate water for human consumption is deplorable.

As the 'mercury rises,' a paralleled increase in the incidence of food-, water- and vectorborne illnesses has also been documented, and these have been at least partially attributed to a number of deaths in recent years (7, 8). Among the changes being observed in the Canadian climate is a rise in the incidence of violent storms, which can lead to temporary 'pulses' in local water contaminants and bacteria that increases the risk of becoming ill (9-11). Even more worrisome is that this only appears to be the beginning since the global shift in climate and temperatures are expected to worsen in the coming years, since the world appears to be committed to several more decades of warming (9).

An equally worrying trend has also been observed in air quality and the potentially fatal exacerbation of several chronic health conditions including asthma, chronic obstructive pulmonary disease (COPD), lung cancer and cardiopulmonary-associated conditions, to name a few (12). Although the etiology of many of these conditions is complex and is likely attributable to other causes at present, there is no doubt those acute changes in outdoor air quality, such as smog episodes, increases patient morbidity and mortality. Despite the existence of strict Canadian policies with regards to the use of fossil fuels, other nations have lagged behind and are severely suffering from their lack of intervention (13-15). Moreover, these bothersome trends are unlikely to disappear anytime soon, as these developing nations are also struggling against the slumping global economy and are trying to rapidly restore their own economies without any long-term regards to the future consequences.

As governments around the world attempt to implement new policies that aim to stimulate the global economy, it is worth asking where the environment fits into these plans. For example, back in 1992, the Kyoto protocol brought the hope of governmental engagement for a better planet. However, the emerging dichotomy between keeping the economy afloat and respecting the clauses of the treaty have lead to the controversial ratification of the allegiance to the Kyoto treaty by some of the signatories, such as the European Union and Canada, to name a couple. However, given that a nation's economic status is dependent on the wellness of their workforce, the impact of environment on health should not be overlooked. More importantly, is the healthcare system ready in terms of financial and main-d'oeuvre resources, to tackle the increase incidence of illness related to environmental deterioration? As such, we urge our readers to consider the importance of developing governmental policies that not only address the present economic crisis, but we would also encourage you to consider the long-term benefits and advantages that might be achieved in both health and environment through the implementation of sustainable programs.

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ORIGINAL ARTICLE

Retrospective review of two-port thoracoscopic (VATS) wedge bullectomy and lung wedge biopsy

Jimmy Bejjani*, Guillaume Couture, Juan-Francisco Asenjo, Marco Sirois, Chantal Sirois, Christian Sirois

ABSTRACT: ***Background*: Video-assisted thoracoscopic surgery (VATS) involving wedge resection of bulla and lung biopsy can be done by two or three-port incisions. Controversy exists as to which approach is superior. We communicate our experience with two-port VATS for these procedures.** ***Methods*: We retrospectively analyzed the charts of all patients who underwent a VATS procedure by two-port incisions from July 2001 to July 2007 by two thoracic surgeons (S.C., S.C.) We included in the study all patients who underwent wedge resections for primary or secondary spontaneous pneumothorax and biopsies for pulmonary infiltrates and small nodules.** ***Results*: A total of 319 patients' charts were examined, and 217 of whom had undergone two-port incisions fitted in the inclusion criteria. There were 136 (65.7%) males and 81 (37.3%) females with a mean age of 47 years. Pneumothorax was the main diagnosis for 98 (45%) patients, followed by pulmonary infiltrates for 69 (32%) patients and lung nodules for 50 (23%) patients. The mean operative time and the number of post-op days for chest tube removal and to discharge home in each group have also been recorded. There were few post-operative complications, such as 11 (5%) cases of persistent air leak, 11 (5%) cases of transient fever of unknown origin, 3 (1.4%) cases of pneumonia, 3 (1.4%) cases of bleeding within, one reoperated, and 1 (0.46%) case of C. difficile colitis. The 30-day mortality was 0%.** ***Conclusion*: The thoracoscopic (VATS) wedge biopsy via two-port incisions is a safe operation for patients presenting with pneumothorax or requiring a lung biopsy. A two-port approach seems to be a reasonable alternative to three-port incision procedures for these types of diagnosis, regarding post-operative pain and cosmetic benefits particularly for young patients.**

KEYWORDS: VATS, pneumothorax, bullectomy, thoracoscopy, pleurodesis, pulmonary nodule, pulmonary infiltrates, lung neoplasms.

INTRODUCTION

Lung cancer incidence was 73,6/100,000 in 2004 in the United States (1), and spontaneous pneumothorax are more rare. Between 1991 and 1995, the rate of admissions to UK hospitals for both primary and secondary spontaneous pneumothorax was 16.7 per 100,000 men per year and 5.8 per 10,.000 women per year (2). One diagnostic and therapeutic alternative to thoracotomy is video-assisted thoracoscopic surgery (VATS), allowing wedge bullectomy and lung wedge biopsy while reducing pain by smaller incisions and leading to shorter hospital stay. VATS can be performed by three, two and even one-port incisions. Controversy exists as to which approach is superior (3,4). At our institution, three surgeons use either two-port or three-port procedure VATS but otherwise the same technic. They do not use one-port. We have reviewed our experience with two-port VATS over the last 6 years to determine wether this approach can be regarded as safe.

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PATIENTS AND METHODS

Patients

The charts of all patients who underwent a thoracoscopic procedure by two-port incisions from July 2001 to July 2007 by two thoracic surgeons were

reviewed. We included in the study all patients who underwent wedge resections for spontaneous pneumothorax and wedge biopsies for pulmonary infiltrates and small nodules (<1.5 cm). The exclusion criteria were high pre-operative O2 requirement (FiO2>0.5), large nodules (greater than 1.5 cm diameter), diffuse severe emphysema, giant bulla, and those who were converted to open surgery for any reason.

Data collection

Retrospective data collection includes comorbidities, surgical treatment received, duration of surgery, duration of chest tubes, hospital length of stay (LOS), post-operative complications and analgesia.

Surgical procedure

All patients were operated using the same technique. Under general anesthesia with double lumen intubation, the patient was placed on the lateral decubitus position to expose the left or right chest. A small 2cm transverse skin incision was performed on the lateral and lower aspect of the chest. A tunneled dissection was made superiorly for subsequent chest tubes. The 8th or 9th intercostal space was opened. The lung was deflated. A second thoracoscopic port incision was performed more superiorly and anteriorly or posteriorly.

Following that, a 10-mm, 0' thoracoscope (Karl Storz) with a working channel was introduced into the pleural cavity through the first incision. Careful inspection of the pleural space was performed.

For bullectomy and pleurectomy or pleurodesis, the apex of the upper lobe, having blebs, was grasped through the working port of the scope and an Endo GIA-45 stapler (3.5mm green cartridge Ethicon®) was used through the second port. The upper segment of the lower lobe was carefully inspected and blebs were resected using the same technic.

Regarding lung wedge biopsy for nodules or infiltrates, limited small wedge resections were performed using an endograsper and an endoGIA-45 4.8mm stapler. The wedge resections for biopsy were performed in different areas of the lung to obtain a good sampling.

Combined apical pleurectomy and mechanical pleural abrasion was performed for pleurodesis, on the anterior, lateral, and posterior aspects of the chest wall. For some elderly patients with chronic obstructive pulmonary disease, following the mechanical abrasion, talc poudrage was used to achieve optimal pleurodesis. Following irrigation and suction with normal saline, a 32 French chest tube was placed posteriorly to the lung up into the apex through the camera port. The lung was reinflated. All the incisions were closed using 0 Vicryl sutures stitched on the subcutaneous tissue and Monocryl 4-0 subcuticular on the skin. Intercostal block with bupivacaine 0.25 with epinephrine was done in the intercostal space where the trocar and the chest tube have been placed.

RESULTS

We reviewed the charts of 319 patients and a total of 217 patients had undergone two-ports incisions and fit in the inclusion criteria; all remaining cases corresponded to any of the exclusion criteria. There were 136 (65.7%) males and 81 (37.3%) females with a mean age of 47 years (range 14-84).

General demographic data are shown in table 1.

The operative time, LOS, chest tube requirement time duration are summarized in table 2.

We noticed that 16% of primary spontaneous pneumothorax (PSP) cases showed postoperative complications, 19% for secondary spontaneous pneumothorax (SSP), 14% for pulmonary nodules and 12% for pulmonary infiltrate.

The most common postoperative complications were

Diagnosis	N	%	♂	♀	Mean age (yr)	Range (yr)
Primary spontaneous pneumothorax	81	37.3	66	15	29.3	17-83
Secondary spontaneous pneumothorax	18	8.3	14	4	52.7	14-79
Pulmonary infiltrates	68	31.3	33	35	64.4	18-83
Pulmonary nodules	50	23	23	27	50.4	23-81

Table 1: Demographic data.

Diagnosis	PSP	SSP	Pulmonary nodules	Pulmonary infiltrates
Operative time (min)	75 (35-135)	88 (51-145)	74 (50-115)	69 (35-130)
Chest tube requirement time duration (day)	3.85 (1-12)	3.67 (1-6)	2.34 (1-9)	3.22 (1-13)
LOS (day)	4.79 (2-40)	5.94 (2-17)	3.20 (1-9)	4.78 (2-20)

Table 2: Operative time, chest tubes duration and LOS.

11 (5%) cases of persistent air leak, 11 (5%) cases of transient fever peak of unknown origin, 3 (1.4%) cases of pneumonia, 3 cases (1.4%) of postoperative bleeding, and 1 (0.46%) case of C. difficile colitis which has resolved. There were no cases of wound/cellulitis, empyema, arrhythmia or cardio-vascular event. Only three cases of primary spontaneous pneumothorax needed a reoperation for bleeding, persistant air leak and a recurrency. The 30-day mortality was 0%.

Within the 98 patients operated for pneumothorax, 82 (83.7%) underwent pleurodesis by mechanical abrasion, 6 (6.1%) by talc poudrage, and 10 (10.2%) received no pleurodesis. Within the 69 patients operated for infiltrates, 1 (1.4%) underwent pleurodesis by mechanical abrasion, 3 (4.3%) by talc poudrage and 65 (94%) received no pleurodesis (figures 1 and 2).

DISCUSSION

VATS is known for being both an effective diagnosis and therapeutic tool employing minimally invasive techniques. It became involved in the diagnosis of idiopathic interstitial lung disease (5), and the staging of lung nodules (6) while allowing a simultaneous assessment of the pleura. It also facilitates the treatment of pneumothorax by wedge bullectomy and pleurodesis. For primary spontaneous pneumothorax, it has even been demonstrated effective and safe for the first episode (7).

Our cohort data suggests that the average operative time is proportional to the number of postoperative days to remove chest tubes and discharge home if no postoperative adverse event occurs. This constatation excludes the cases involving pulmonary infiltrates for which the longer length of stay is due to the pre-operative disease.

Compared to other VATS studies for spontaneous pneumothorax and indeterminate interstitial lung disease, our data shows good results regarding operative time, chest-tube drainage, and postoperative hospital stay.

For mean operative time, studies state values as 57±19 minutes (8), 67.9±16.7 minutes (5), and 129 minutes (9). For pleural drainage, studies show mean duration as 1.4 days (range 1-7) (10), 4.1 days (9), 5.8±1.2 days (2), and 6.0±4.7 days (5). For postoperative hospitalization, values were published for 2.4 days (10), 4 days (9,11), 5 days (12), 7.7±1.6 days (8), 7.9±4.7 days (5), and 9.5 days (9).

Compared with previous studies in terms of postoperative mortality and morbidity, our sample of patients who underwent two-ports surgery for VATS had very good results.

Regarding 30-day mortality, studies often depicts no cases (5,7-9,12-14) or rates as low as 0.5% (15), 0.8% (16), 1.3% (17) and 3.6% (18). This last increased rate was seen for secondary spontaneous pneumothorax, due to diagnosed pulmonary pathologies as emphysema. Higher rates are present for postoperative complications, for which increasing factors include extreme age range and preoperative comorbidities. Studies depict morbidity of 9.6% for nodules (15), 1.7% (13), 25.4% (17), and 27.4% (8) for primary spontaneous pneumothorax, and 25% (13) and 76.9% (17) for secondary spontaneous pneumothorax. In previous reviews, persistant air leak was seen for 10% to 11.5% of procedures (9,17), pneumonia in up to 6.7% (17), bleeding in 1.6% (19). Those rates are equivalent or higher to ours. Moreover, others describe arrythmia (17), empyema (17), and wound infection (13) that didn't occur in our cohort.

To minimize these complications, authors recommend a close monitoring in the post-operative care unit and on the ward. Vital signs, chest tubes drainage and incision wounds should be checked by the surgical team in morning rounds, and twice a day by nurses. Moreover, chest radiographs and complete blood count may be of particular interest if patients are symptomatic. Prevention of C. difficile infection is also important with a judicious use of antibiotics and isolation when necessary.

Interestingly, during the post-operative days, patients operated for lung infiltrates consumed more morphine (65.3 mg) than patients who underwent the surgery for lung nodules and pneumothorax (48.4 mg and 42.1 mg, respectively).

We noticed that the practice of pleurodesis did not significantly increase the use of narcotics, despite the earlier notion that pleurodesis increase pain in an important way. Post-operative morphine administration levels in pneumothorax cases whom surgery included mechanical abrasion illustrate an average difference of less than 10mg in post-operative day 1 and 2 (figure 1). This value spread is negligeable. A study also suggested that additionnal mechanical pleurodesis has no disadvantages versus bullectomy alone in terms of worsening post-operative chest pain or pulmonary function (20).

Chemical talc pleurodesis appears to decrease the need for post-operative morphine. In our cohort, postoperative morphine administration levels in cases of pulmonary infiltrates were much greater for patients receiving no pleurodesis than for those receiving chemical talc pleurodesis. However, this included only 3 patients and is therefore highly suseptible to hazard (figures 1 and 2) .

CONCLUSION

We conclude that thoracoscopy (VATS) via two-port

incisions is a safe and efficient procedure for patients presenting a pneumothorax or requiring a lung biopsy. Our complication rate is similar or lower to the rates of three-port thoracoscopy. This technique is arguably superior to three-port incisions based on the finding that it may decrease the postoperative pain and neuralgia risks, and presents obvious cosmetic benefits particularly for young patients. A comparative study with three-port incisions is warranted to elucidate this controversy.

ACKNOWLEGMENT

This review project was partially funded by the Dr. Clarke K. McLeod Memorial Scholarship Fund in 2007.

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ORIGINAL ARTICLE

Psychiatry as a career: A survey of factors affecting students' interest in Psychiatry as a career

Mubashir Aslam*, Tahir Taj, Arif Ali, Nasira Badar, Farzan Saeed, Muhammed Abbas, Saad Muzaffar, Bilal Abid

ABSTRACT: The objectives of this study were to determine the characteristics of medical students and graduates interested in choosing psychiatry as a career and the obstacles in choosing this field of medicine. Two private and two public medical institutes were surveyed from June 2007 to August 2007. A self-administered questionnaire was distributed to third, fourth and final year students and to medical graduates doing their internship in these four medical institutes.A total of 909 medical students and graduates participated in the study. Seventeen percent of participants responded positively regarding their interest in psychiatry as a career. Significantly higher proportion belonged to private medical institutes (14% vs. 24%, P-value =0.001). There was no significant difference in reporting interest for psychiatry in regard to age, sex, year in medical school and whether or not the participant had done a psychiatry ward rotation. However significantly higher proportion of participants (22%, n=43) were reporting their interest in the field of psychiatry who had done more than a month long psychiatry ward rotation as compared to those participants (14%, n=54) with less than a month or no psychiatry rotation (P-value=0.01). More students were reporting their interest in psychiatry with a family history of psychiatric illness as compared to without family history (24% vs 16%, P-value=0.03). In conclusion, students and graduates with more than a month long rotation in psychiatry, studying in private medical colleges and with a family history of psychiatric illness were more interested in choosing psychiatry as a career.

KEYWORDS: Psychiatry in Pakistan, Career in Psychiatry, medical students in Karachi.

INTRODUCTION

Mental health is an ignored subject in the field of medicine and in the area of public health, and less 1% health budget is spent on mental health problems in developing countries (1). This neglect accounts for students' lack of interest in psychiatry and fewer medical students consider psychiatry as a career choice (2) as compared to other medical subspecialties. Furthermore health policy makers and investigators did not give sufficient attention on the issue of students' disinclined attitude towards psychiatry. However since the 1960s, some educational studies have investigated the phenomenon of medical students' interest in the field of psychiatry and their behavior towards mentally ill patients (3).

Pailhez G et al compared the attitude of Spanish and United States medical students toward psychiatry in a cross sectional study (4), which revealed that Spanish students showed a positive attitude towards Psychiatry as compared to U.S. students. Only 6% of Spanish students were considering psychiatry as a career which was slightly higher than U.S. medical students where only 4.5% students were interested in the field of psychiatry. The most common concerns expressed by the students relate to the lack of scientific rigor in psychiatry, is the non-efficacy of treatment, and the psychiatrists' low social status among physicians.

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Similarly in Pakistan, Psychiatry is not considered a popular field of medicine among students (5), and as such Pakistan is also facing shortage of physicians in this medical subspecialty. Even though a Department of Psychiatry have been established in most of the tertiary care teaching hospitals in the country (6), there are only 250 Psychiatrists in Pakistan and these practice mainly in urban settings (7). Data from population-based studies in urban settings revealed that one third of Pakistan's population have anxiety/depression (8). Even though effective treatments are available for most of these disorders (9), there is a shortage of psychiatrists and other trained professionals like psychologists, nurses, and paramedics. The available one Psychiatrist for 0.64 million Pakistanis are absolutely insufficient; in addition a large proportion of Psychiatrists do not have postgraduate qualifications (1, 10). WHO reported that millions are affected by mental illnesses and the incidence is on the continuous rise. As high as 154 million people faces major depression and 25 million suffer from schizophrenia. In addition addiction and substance abuse also contribute a major burden among mental health problems, as many as 91 million people get disorders which are directly or indirectly alcohol related and 15 million by other addictive drugs (1).

Medical graduates with a good attitude towards psychiatry are sometimes unable to pursue their career in this medical subspecialty. Even though some studies have been done in our part of world regarding psychiatry as a career and most of them have tended to identify only attitude of medical students (11-14), yet hindrances in opting for psychiatry as a career have not been studied. Furthermore, most of the studies included medical students and have overlooked medical graduates and interns, who are at critical point of choosing their medical career in a particular specialty. Therefore the objective of this study was to compare medical students and graduates' perceptions around hindrances in choosing Psychiatry as a specialty in Pakistan.

METHODOLOGY

This cross sectional study was conducted in two public (Dow Medical College and Sindh Medical College) and two private medical institutes (Aga Khan Medical College and Ziauddin Medical College) from June 2007 to August 2007 in Karachi. There are three public medical institutes in Karachi and Dow and Sindh Medical College are the two largest public institutes. Average number of student varied from 200 to 250 for each class in these public medical institutes. Aga Khan and Ziauddin medical college were selected out of six private medical institutes in Karachi. There is a significant difference between public and private medical institutions as to the technique of teaching. Some private medical institutions are following a problem based learning system (PBLS) (15), whereas all the public medical institutions follow a conventional lecture based curriculum (LBL). In addition, there are certain postgraduate specialty training programs, like Family Medicine, which is only offered in private medical institutions (16). In Pakistan, medical schools offer a five (5) year program leading to an M.B.B.S (Bachelor of Medicine; Bachelor of Surgery) degree. Basic health sciences are the primary focus of instruction during the first two years, with gradually increasing exposure to clinical rotations over the next three years (15). After graduation, there is one-year compulsory internship in a teaching hospital in order to obtain medical licensure. Fellowship training starts after completing an internship and passing a postgraduate medical exam (16).

The authors developed a self-administered questionnaire in English as all of these medical institutes have English as an official teaching language. The questionnaire included demographics, undergraduate courses, satisfaction in medical profession, and first, second and third career choices of medical students (questions regarding a particular field of medicine will be reported separately). The questionnaire was kept anonymous to maintain confidentiality of the participants. Pre-testing of questionnaire was done on 30 participants from each of the four medical institutes to determine response rate and applicability of the tool; changes were made in the questionnaire accordingly (unpublished data). The same questionnaire was used for data collection from all four medical institutes.

Only third, fourth and final year medical students and house officers were included in this study. First and second year students were excluded because of little exposure to clinics in beginning years of medical studies and less number of students were able to report their commitment for any particular medical specialty. After seeking verbal consent, data collectors distributed self-administered anonymous questionnaires to medical students after lectures, tutorials and PBL (Problem based learning) in medical colleges and were recollected after few minutes. To target house officers, questionnaires were distributed and collected in different wards of the attached teaching hospitals within these four medical institutes. The department of Community Health Sciences, Sindh Medical College issued study approval. An information sheet was attached with each questionnaire to provide project details, rights of the participants and suggesting that filling the questionnaire implies informed consent.

Data were entered and analyzed in SPSS version 15

(17); categorical variable of self-reporting interest in choosing Psychiatry as a career was the defined outcome. Interested in choosing Psychiatry is defined as "those who find the subject interesting to take as a career however may not actually be taking it as postgraduate specialization field". Chi-square and t-test were applied for categorical and continuous variables respectively to test the statistical significance at 95% confidence level.

RESULTS

A total of 909 medical students and graduates participated in the study (response rate was 90% of individuals who received questionnaire), of which 285 (31%) belonged to one of the two private medical institute and 624 (69%) participants were part of public medical institute in Karachi. Age of participants ranged from 19 to 28 years (mean=22 years, s.d=1.7). Six hundred and fifty (71%) participants were male. Overall 157 (17%) participants reported their dedication in opting psychiatry as a career including 67 (24%) of individuals from private medical institutes and 90 (14%) from public medical institutes showing that significantly higher proportion of individuals were reporting their interest in psychiatry in private institute as compare to public medical institutes (P-value=0.001). There was no significant difference in reporting interest for Psychiatry with regards to age (mean=22.1±1.8 vs. mean=22.3±1.9, P-value=0.28), sex (15% vs. 18%,P-value=0.38), year of study (3rd yr=22%, 4th yr=17%, 5th yr=14%, Interns=17%, P-value=0.17) and whether or not the participant had done a psychiatry ward rotation (17% vs. 18%, P-value=0.68). However a significantly higher proportion of participants (22%, n=43) were reporting their interest in the field of Psychiatry who had done more than a month long psychiatry ward rotation as compare to those participants (14%, n=54) with less than a month rotations (P-value=0.01). Furthermore it was noticed that 24% (n=27) of participants reported their interest in psychiatry who had a family history of psychiatric illness while only 16% (n=126) were reporting their interest in Psychiatry with no family history revealing a significant difference in two groups (P-value=0.03) [Table 1].

The evaluation of hurdles in choosing psychiatry as a career in private and public institutes demonstrated that mean score of the component "stressful conditions with patients" was highest among the participants of both private (mean=3.4, SD=1.5) and public medical institutes (mean=3.3, SD=1.4). However mean scores of each of the other components was higher among the participants of private institutes as compared to the medical students and graduates in Government medical institutes given rise to the total sum of mean scores are 13.9 and 14.7 for public and private medical institutes respectively [Table.2].

DISCUSSION

This study results revealed that 17% of medical students and graduates reported interest in choosing Psychiatry as a career. However a much higher proportion of students belonged to private medical education system who were reporting interest in psychiatry. Mandatory undergraduate courses of psychiatry in private medical schools might be the reason for this difference, as it is mostly taken as an optional subject in public medical institute in Karachi. This study also unmasked the finding that is consistent with Walters et al. that the higher proportion of medical students and graduates were reporting positive interest in psychiatry who had taken psychiatry as undergraduate subject (18). Furthermore it has been determined that those participants who had done more than a month of clinical rotation in psychiatry were reporting a significantly positive response towards choosing a career in psychiatry. These results are consistent with other studies including a prospective study to evaluate the effects of a psychiatry rotation on the attitude of medical students towards psychiatry (19-21). Moreover the results regarding a positive association between choosing psychiatry as a career and a family history of mental illness is also consistent with other studies (22). Another study shows that positive educational experiences as well as personal experiences increase the probability of students' recruitment into the field of psychiatry. Nevertheless it is still ambiguous whether the focus should be on increasing the educational level regarding psychiatry as a subject and clinical rotation, or if it should be on issues which are related to the incentives in this field including career opportunities, income potential and establishment of better structure for the post graduate studies programs in the field of psychiatry (2). Results of Raja Gopal et al. and Olaf et al. revealed that there is no association of gender, age and year of study with higher interest of students in choosing Psychiatry as a career that is consistent with the results of this study but with a larger sample size (2, 22).

Hindrances in choosing Psychiatry as a career were also evaluated in this study as studies have shown that for most of the students, psychiatry is the last choice to be taken as postgraduate training even though students consider it an intellectually challenging field (1). A 5 item Likert questionaire was used to quantify the major factors responsible for the lower recruitment in psychiatry in our circumstances. Four of the items including "less incentives in the field", "less popularity

among other medical specialists", "stressful conditions with patients" and "less career opportunities" were used for evaluation in other studies as well. However a fifth component which was "discouragement from family" was included in this questionnaire because of the local scenario in Asian countries particularly Pakistan, where families also play a crucial role regarding career decision of students. Most of the medical students were concerned with stress in the field of psychiatry due to prolong contact with Psychiatric patients which was also determined in a study by Cutler JL et al (23).

One of the limitations of this study was that structured items were given in the questionnaire for evaluating hindrances in psychiatry as a career even though there

Variables	Total	Interested for career in Psychiatry				Chi-square	P-value
		Yes		No			
		n	%	n	%		
Gender							
Male	650	116	18	534	82	0.76	0.38
Female	253	39	15	214	85		
Medical institute							
Private	285	67	25	218	75	11.3	0.001*
Public	624	90	14	534	86		
Socioeconomic status							
Lower Middle class	123	22	18	101	82	7.38	0.02*
Upper Middle class	668	106	16	562	84		
Upper class	96	26	27	70	73		
Self Satisfaction							
Satisfied in Medical Profession	715	121	17	594	83	0.33	0.52
Not satisfied	176	33	19	143	81		
Clinical posting in Psychiatry							
Yes	583	97	17	486	83	0.16	0.68
No	282	50	18	232	82		
Months of Psychiatry rotation							
<1 month	383	54	14	329	86	5.6	0.01*
>1 month	197	43	22	154	78		
Studies Psychiatry in undergraduate							
Studied	488	96	20	392	80	4.7	0.01
Not studied	409	58	14	351	86		
Year in Medical School							
Third year	215	47	22	168	78	4.9	0.17
Fourth year	283	47	17	236	83		
Final year	215	30	14	185	86		
House officer	196	33	17	163	83		
Family History							
Psychiatric illness in Family	113	27	24	86	76	4.2	0.03*
No Psychiatric illness	781	126	16	655	84		
*Significant P-values							
Data is shown as number followed by percentage.							

Table 1: Characteristics of Medical students and graduates (participants) in regard to interest in Psychiatry

could be more concerns, which would prevent them from choosing this field. However this can be explained on the basis that response rates were expected to decline if these questions were left open ended because of the time required to write answers. Another limitation was that the outcome variable was self-reported interest in psychiatry as a career so there could be variations in expected and observed responses. Nevertheless the variations were expected to be minimal by obtaining similarity in data from comparable institutes including two private and two public medical institutes. The reason for taking this outcome variable instead of analyzing highly committed students who wrote psychiatry as a first career choice in open ended question, which were estimated to be only 2.5% in total (Data not shown), was that because with a larger sample the characteristic of students interested in psychiatry as a career can grossly be identified which may increase interest towards psychiatry as a career compared to the control population. It was assumed that increasing students interest towards this field could eventually increase the recruitment of students in the field of Psychiatry. Selection bias may have been a factor since more students were reporting interest in psychiatry who had more than a month rotation in the psychiatry ward, however it was not determined whether they had selectively done it or it was a mandatory rotation.

The strength of this study includes having a large sample size and inclusion of house officers (interns) because they are the one who are at a critical stage in deciding about their medical specialty and can better report their interest in and commitment to a particular career.

CONCLUSION

Students and graduates who have had more than a month long rotation in psychiatry, studying in a private medical college and a family history of psychiatric illness are more interested in choosing psychiatry as a career. Stressful working conditions with patients ranked highest as a hindrance in not choosing psychiatry as a career. In addition appropriate incentives in the field of psychiatry in terms of money and career opportunities are lacking in Pakistan. More structured post graduate programs in psychiatry with better guidelines for the career opportunity in this field may help raise enrollment in psychiatry. Furthermore there is an immediate need to make psychiatry a mandatory undergraduate subject in all of the medical institutes in Pakistan.

ACKNOWLEDGMENT

Authors acknowledge the significant cooperation of the administrative staff of in the study settings for the permission and facilitation of data collection by students.

DECLARATION OF INTEREST

Authors declare no conflict of interest with any organization or funding agencies.

CONTRIBUTION OF AUTHORS

Dr Mubashir and Dr Tahir started the initial planning of the project and worked until the final manuscript submission. Dr Ali Abbas, Dr Saad Muzafar, Dr Nasira Badar, Mr Farzan Saeed and Dr Bilal Abid were involved in the collection, entry and analysis of data and helped write the initial draft of the manuscript. Arif Ali supervised data management and all the statistical analysis.

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Rank	Components	Public Institute M ± SD(n)	Private Institute M ± SD(n)	P-value*
1	Stressful condition with patients	3.4± 1.5 (543)	3.3± 1.4 (263)	0.4
2	Less career opportunities	2.8± 1.4 (525)	3.1± 1.3 (260)	0.02
3	Less popularity among other specialist	2.8± 1.5 (523)	3.0± 1.3 (262)	0.05
4	Discouragement from family	2.7± 1.6 (538)	2.8± 1.6 (258)	0.26
5	Less incentive (money)	2.2± 1.4 (520)	2.5± 1.4 (256)	0.03

Note : Data only for those who had indicated experience (1=least responsible factor and 5 =most responsible factor), * t-test was applied

Table 2: Hindrances in choosing Psychiatry as a career

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ORIGINAL ARTICLE

Study of prescription of injectable drugs and intravenous fluids to inpatients in a teaching hospital in Western Nepal

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ABSTRACT: Unnecessary, excessive and poor injection practices in the South East Asia region (including Nepal) have been observed previously. The authors aim to study prescription of injectable drugs to inpatients in a teaching hospital in Western Nepal. Prescription of injectable drugs (IDs) and intravenous fluids (IVFs) to inpatients discharged from the wards of the Manipal Teaching Hospital during 1st January to 30th June 2006 was studied. The mean number of drugs, IDs and IVFs administered, median cost of drugs and of IDs/IVFs per prescription calculated. Comparison of ID/IVF use in the four major hospital departments (Medicine, Obstetrics and Gynecology, Pediatrics and Surgery) was done. The administration of IDs/IVFs and injectable antimicrobials were measured in Defined Daily Dose (DDD)/100 bed-days and of Intravenous fluid in Liters (L)/100 bed-days.Of the 1131 patients discharged, 938 (82.94%) patients received one or more IDs/IVFs. The mean number of drugs, IDs and IVFs prescribed were 8.75, 4.72 and 1.42. Median cost of drugs and IDs/IVFs per prescription were 8.26US$ and 5.12US$ respectively. IDs/IVFs accounted for 81.37% of total drug cost. The most commonly used ID, injectable antimicrobial and IVF were Diclofenac (19.3 DDD/100 bed-days), Metronidazole (7.68 DDD/100 bed-days) and Dextrose normal saline (8.56 L/100 bed-days), respectively. The total IVF consumption was 24.25 L/100 bed-days. Significant differences between departments were observed ($p<0.05$). In conclusion, the use of IDs/IVFs was higher compared to other studies. Interventions to improve IDs/IVFs prescribing practices may be required.

KEYWORDS: defined daily dose, drug utilization, injectable drugs, inpatients, Nepal, rational use of medicines.

INTRODUCTION

Drug utilization research is defined as research on "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" and has the principal aim of facilitating the rational use of drugs (1). In developing and transitional countries (including Nepal), some 16 thousand million injections are administered each year – a rate of 3.4 injections per person per year (2). The majority of injections are unnecessary (3). Reuse of injection equipment in the absence of sterilization was highest (75%) in the South East Asia Region (consisting of nine countries including Nepal) of the World Health Organization (WHO) (2). The combination of injection overuse and unsafe practices creates a major route of transmission for Human Immunodeficiency Virus (HIV), Hepatitis and other blood borne pathogenic infections (2).

In order to compare drug utilization among different countries and even among health institutions within a country, the ATC and DDD concepts were introduced (4). The Anatomical Therapeutic Chemical (ATC) classification system represents a common language for describing the drug assortment. The DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults (4, 5). It provides a fixed unit of measurement independent of price and formulation.

A study in the Intensive Care Unit (ICU) from a teaching hospital in Western Nepal showed that 52.8%

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of drugs were administered by the parenteral route, and more interestingly 74% of patients were given an intravenous fluid (IVF) during the period of their ICU stay (6). A prospective, cross-sectional study of a tertiary care teaching hospital in Eastern Nepal reported that 77.7% of the in-patients were prescribed injectable drugs which constituted 40.4% of the total number of drugs (7). These studies were either confined to a particular department or concentrated on a particular group of drugs.

In view of the high prevalence of use of injectable drugs (IDs) and intravenous fluids (IVFs), there is an urgent need to study their utilization. These data are scant in Nepalese in-patient populations. Knowledge on how IDs/IVFs are being prescribed and used will be of immense help in initiating a discussion on their rational use and suggesting measures to improve prescribing.

The present study was carried out to obtain baseline data on prescription of IDs and IVFs to the inpatients. The objectives of the study were to:

1) Obtain relevant demographic information of inpatients of Manipal Teaching Hospital (MTH) prescribed IDs/IVFs during the study period.
2) Obtain information on the patterns of prescription of IDs/IVFs
3) Calculate DDD/100 bed-days of the ten most commonly used IDs and injectable antibiotics.
4) Measure IVF utilization in liters/100 bed-days.
5) Calculate the proportion of the total drug cost constituted by IDs/IVFs and
6) Analyze and compare the utilization of IDs/IVFs between the MTH's four major departments (Medicine, Obstetrics and Gynecology (OBG), Pediatrics and Surgery).

MATERIALS AND METHODS:

The study was carried out over a six-month period (1st January to 30th June 2006) at MTH, a 700 bedded tertiary care hospital, affiliated with the Manipal College of Medical Sciences (MCOMS) in Pokhara, Nepal. The middle ten days of each English month was selected to minimize the influence of income on hospital visits. The period covered five days before getting salary and five days after getting salary, since most of the Nepalese people get their salary according to the Nepalese month which start around the middle of the English month. To make things clearer, the Nepalese month of Magh 2065 started on January 14th and will end on February 11th 2009.

Records of patients discharged from the various wards of MTH during the study period were obtained from the medical records department (MRD) and analyzed. Inpatients discharged after observation in the Emergency department and from the Ophthalmology ward were excluded. Patients admitted for diagnostic procedures such as endoscopy, hemodialysis etc. and discharged after the procedure was also excluded.

Age, Sex, Address, Hospital (patient) number, Department of Admission, Date of Admission and Date of Discharge of the patient were recorded. For calculating the length of stay, the day of admission was included, while that of discharge was excluded. The diagnosis written in the discharge summary was noted. The name, dose, frequency, duration and route of administration of drugs prescribed during hospital stay were recorded.

The patients were divided into four age groups (0-1, 1-15, 15-60 and >60 years). Analysis of ID/IVF use in the four major departments was also done separately. The department of Medicine runs the Medicine Outpatient department, Medicine wards, the semi-ICU and the ICU of the hospital. The mean number of drugs, IDs and IVFs administered and their average cost were calculated. The proportion of total drug cost and of total drugs (both injectable and non injectable drugs prescribed to these patients) constituted by IDs/IVFs were calculated. The cost was calculated by using Health Information System (HIS), (developed by the Manipal Corporate office in Bangalore, India) a computer software program used by the hospital pharmacy of MTH. The cost refers only to the cost of drugs and the cost of administration and related fees was not taken into consideration. The cost was calculated in both Nepalese rupees and US dollars (one US dollar (US$) = 78.5 Nepalese rupees (NRs) on 22nd January 2009). The cost was recalculated to give the latest conversion figures relative to the US dollar.

The drugs were classified according to the ATC system and utilization of IDs was measured in DDD/100 bed-days and of IVFs in L/100 bed-days. Injectable drugs (IDs) refer to drugs which were administered by injection to the patients of the study. Drugs injected into a peripheral intravenous line were also considered as IDs.

The DDD/100 bed-days of the ten most commonly used IDs were calculated using the following formula (4):

DDD/100 bed-days = (Drug consumption in the study period (mg) × 100)/ (Assigned DDD (mg) × Period of study × Bed strength × Average occupancy)

The time period of study was sixty days. There were 583 beds in the wards included in the study and the average occupancy index was calculated to be 0.299.

Intravenous fluid (IVF) utilization was calculated using the following formula:

(Liters/100 bed-days) = (Consumption of the particular IVF during the study period (L) × 100)/ (Period of study × Bed strength × Average occupancy)

For statistical analysis Statistical Package for Social Sciences (SPSS) version 10.0 for windows (SPSS Inc., Chicago, Illinois, United States) was used. One way ANOVA was applied to compare means of various parameters of the four major departments and when significant ($p<0.001$) differences were noted, Post hoc Scheff test was applied.

A pilot study of five days duration (11th to 15th December 2005) involving 106 patients was carried out in MTH. The result of the pilot study was not included in the final analysis and was broadly similar to those reported here. The instruments used in the study were standard ones used in previous drug utilization studies.

RESULTS

During the study period, 1131 patients were discharged, of which 938 (82.94%) received one or more injection/s during their hospital stay. Percentage of females receiving injections was slightly higher [481 (51.28% of the total 938 patients receiving injections)] than males. Seventy-six patients were infants (0-1 year), 131 were children (1-15 years), 521 were adults (15-60 years) and 210 were elderly (>60years).

Five hundred and ninety-seven (63%) patients were from Kaski district in which MTH is located. A total of 8203 drugs were prescribed with the mean number being 8.75. IDs/IVFs accounted for 52.8% of the total drugs. Mean number of IDs/IVFs was 4.72. A single ID/IVF was administered to 168 (17.91% of total 938) patients, while 145 (15.46%) received two such drugs. Three or more IDs/IVFs were administered to 625 (66.63%) patients.

The most common conditions for which an ID was prescribed were hypertension (10.77%), chronic obstructive pulmonary disease (COPD) (7.78%), acute gastroenteritis (6.29%) and ischemic heart disease (6.08%).

Of the 938 patients, who received IDs/IVFs, 535 (57.04%) received parenteral anti-microbial therapy. A single injectable anti-microbial (IAM) was given to 252 (47.1%) patients, while 161 (30.09%) received two IAMs. Tables 1 and 2 shows the ATC codes and DDD/100 bed-days of the ten most commonly administered IDs and IAMs in MTH respectively.

A total of 1328 IVFs were administered. IVFs were administered to 682 (72.71%) of the 938 patients. Median number of IVF prescribed was one. The total IVF consumption was 24.25 L/100 bed-days. Table 3 shows the consumption of the most commonly prescribed IVFs. Median duration of stay was five days; median cost of prescription and cost of IDs/IVFs in NRs (US$) were 648.5 ($8.26) and 402 ($5.12). IDs/IVFs constituted around 81.37% of the total drug cost. No significant gender variation in administration of IDs/IVFs was observed, but significant inter-departmental variation was observed (Table 4).

Significant differences in the median duration of stay were found between Medicine and OBG ($p=0.006$) and Medicine and Pediatrics ($p<0.001$) with higher duration of stay in Medicine. The mean number of drugs prescribed in Pediatrics was significantly ($p<0.001$) lower than in Medicine, OBG and Surgery.

IDs/IVFs constituted 40.71% of the total drugs prescribed and 72.58% of the drug cost in Medicine. In Surgery 63.37% of the total drugs prescribed and 74.64% total cost of drugs was due to IDs/IVFs. In Pediatrics and Surgery, 56.71% and 66.78% of total prescribed drugs and 87.26% and 88.78% of the total cost of drugs were due to IDs/IVFs

The mean number of IAMs prescribed in Medicine, OBG, Pediatrics and Surgery were 0.71, 1.72, 1.09 and 1.69, respectively. In Pediatrics, Medicine and Surgery, 51, 48 and 44% of patients, respectively received at least one IAM. Table 4 compares frequency of IAM use in the four major departments. Types of antimicrobials prescribed in the four departments were similar except that coamoxiclav (Amoxicillin-Clavulanic acid fixed dose combination (FDC)) prescription was significantly higher in Medicine than in the other three departments. Ciprofloxacin (32%) and a combination of three anti-microbials (Beta lactams, Gentamicin and Metronidazole) (44%) was prescribed more in OBG compared to the other three departments.

Median number of IVFs prescribed in Medicine, OBG, Pediatrics and Surgery were one, one, one and two respectively. Table 4 compares frequency of prescription of various IVFs in the four departments.

Dextrose normal saline (DNS) was the most frequently administered IVF in the department of Medicine. In Surgery, Ringer lactate (RL) was most frequently administered. But RL and Isolyte P were the most frequently administered IVF in the department of OBG and Pediatrics, respectively.

DISCUSSION

In this study, a total of 938 (82.94%) of the 1131 inpatients, discharged during the study period, received at least one injection during their hospital stay. This result is comparable to that reported from Eastern Nepal (7), where 77.7% of total inpatients had received IDs (note: IVFs were not included). In another study from Ghana, 60% of the patients received one or more injectable drugs (8). This may indicate higher rate of injectable administration in MTH. This maybe a matter of concern and the reasons for this should be

investigated in detail.

The local patients frequently visit MTH for their illness, so the patients receiving injections [597 (63.65%)] were mostly from Kaski district. District wise distribution of patients visiting MTH is similar to that noted in previous studies (6,9) done at MTH. Nepal being a mountainous country, problems of accessibility to health care services is an important issue.

The median duration of hospitalization was five days. In a previous study (10) at MTH, median duration of stay was higher than that reported in the present study (nine days). On comparison between departments, mean duration of stay was highest in Medicine followed by Surgery. In a previous study (6) in the ICU of MTH, the mean ± SD duration of hospitalization was 3.84 ± 3.14 days, which is lower than that reported from the medicine ward (7.89 ± 6.34) in the present study. Once a patient's condition improves, they are shifted to other wards and this may be the reason for shorter ICU stay. The patients are generally unwilling to stay in the hospital after IDs have been stopped (11, *Personal observation of the authors and other healthcare providers*). Economic considerations may be partially responsible for the desire to continue further treatment at home (11). Decreased use of IDs/IVFs will decrease the duration of stay and the costs associated. As stated previously (11) early switchover to oral preparations should be considered. Formulation of standard treatment guidelines and an antibiotic use policy in our hospital is in progress.

The mean number of drugs administered was 8.75. In a study from eastern Nepal (7), mean number of drugs was 5.3 and this figure would have been higher if IVFs were counted as drugs. A study by Shankar PR et al (10) in MTH reported the mean number of drugs to be 7.41, which is less than this study. Another study in Ghana (8) showed an average of 3.6 drugs prescribed per patient. Increased administration of IVFs may be a factor partly responsible for the increase in the mean number of drugs. The average number of drugs should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance and hospital cost (12).

The average number of drugs was significantly higher in OBG (10.6) compared to the other three departments. Normal delivery and Lower Segment Cesarean Section were the most frequent clinical conditions for the admission to the OBG ward. In these conditions, multiple drug prescribing was common. Prescribing of more than one antimicrobial is also more frequent in OBG. In Medicine, the mean number of drugs was 9.56 which is less than that reported from Tribhuvan University Teaching Hospital (13) but higher than that reported from Harare (14). Elderly patients and patients

Name of Injection	ATC Code4	Frequency	% of patients prescribed (N=938)	DDD/ 100 bed-days
Diclofenac	M01A B05	228	24.31	19.3
Ranitidine	A02B A02	212	22.6	15.65
Metronidazole	J01X D01	169	18.02	7.68
Gentamicin	JO1G B03	159	16.95	3.53
Ampicillin	J01C A01	147	15.67	5.22
Cefotaxime	J01D A10	147	15.67	2.41
Metoclopramide	A03F A01	128	13.65	3.65
Promethazine	R06A D02	115	12.26	6.86
Tramadol	N02A X02	106	11.3	2.11
Pethidine	N02A B02	102	10.87	0.58

Table 1: ATC codes and DDD/100 bed-days of the ten most commonly used injectable drugs (IDs) in the study

Name of Anti-microbial	ATC Code4	Frequency	% of patients prescribed (N=535)	DDD/ 100 bed -days
Metronidazole	J01X D01	169	31.59	7.68
Gentamicin	JO1G B03	159	29.72	3.53
Ampicillin	J01C A01	147	27.48	5.22
Cefotaxime	J01D A10	147	27.48	2.41
Ceftriaxone	J01D A13	75	14.02	3.66
Ciprofloxacin*	J01M A02	71	13.27	3.77 (2.41 O; 1.36 P)
Cloxacillin	J01C F02	64	11.96	3.15
Coamoxiclav	J01C R02	47	8.79	7.26
Amikacin	J01G B06	43	8.04	1.25
Cefazolin	J01D A04	33	6.17	0.35

Table 2: ATC codes and DDD/ 100 bed-days of the ten most commonly used injectable anti-microbials (IAMs) in the study.
*A single patient may have been prescribed more than one injectable preparation.

with multiple conditions comprised the majority of patients being treated in the Medicine wards. This might be the reason for the greater average number of drugs in Medicine. In this study, it has been found that significantly lower number of drugs were used in Pediatrics (5.43) compared to other departments. Even though mean number of drugs prescribed in Pediatrics was less, the value is higher than the mean of 3.45 reported in a previous Zimbabwean study (15). But the result is comparable to the previous studies (9, 16) done in Nepal.

Of the total drugs prescribed, 53.98% were IDs/IVFs. This is very similar to that observed in a previous study (6) in MTH but higher than that reported from a study from eastern Nepal (7). In the present study, 17.91% patients were administered a single injection, while 15.46% were administered two injections. The average number of injectable drugs should be kept as low as possible, to reduce poly-pharmacy, cost and hazards associated with the practice of injectables (17,18). Mean number of injections administered was lowest in Pediatrics followed by Medicine. But mean number of IDs used is higher than that observed previously (1.68) (16). The percentage of patients receiving IVFs was 69.96% in Medicine (lower than that reported earlier) (13). Among the four departments, OBG administered IVFs to highest percentage of patients (82.65%). The median number of IVFs used was higher in Surgery [2] compared to the other three departments. This is less than the median number of IVF prescribed [3] in a study from Spain (19). The utilization of IVF was 24.25 L/100 bed-days which is similar to the utilization in the ICU (6). Although DNS was the most commonly prescribed IVF in the MTH and in Medicine department, RL was the most frequently administered IVF in surgery and OBG. In OBG, RL was used as a vehicle to administer Oxytocin. This is different from that reported in other studies (20,21). The first study (20) was carried out among post-operative surgical patients while the second studied various fluid maintenance therapy regimens in adult inpatients admitted to the general surgery ward over a one-year period. In a hospital in Serbia, Europe utilization of IVFs varied from 89 to 94 DDD/100 bed-days (22). Further studies on IVF utilization are required in MTH. An old study had looked at use of IVF among medical inpatients in hospitals in the United States, Scotland, New Zealand, Israel and Canada (23). Wide variations in the use of IVFs were noted. The use was maximum in US and least in Scotland and Israel. The percentage was 53.7% in the hospital with highest use. The present study shows a use ofa round 70%. The study (23) was published in 1977 and the passage of time makes it difficult to draw conclusions.

Type of IVF	Frequency	% of Total IVFs (N=1328)	% of patient receiving injection (N=938)	Liters/ 100 bed-days
Dextrose Normal Saline (DNS)	387	29.14	41.26	8.56
Ringer Lactate (RL)	330	24.85	35.18	5.77
Normal Saline (NS)	260	19.58	27.72	5.3
5% Dextrose	132	9.94	14.07	2.29
Isolyte P	85	6.4	9.06	1.27
10% Dextrose	76	5.72	8.1	0.82
Mannitol	24	1.81	2.56	0.12
Others	34	2.56	3.62	0.12
Total	1328*	100	-	24.25

Table 3: Utilization of Intravenous Fluids (IVFs)

Median cost of drugs and IDs/IVFs per patient was 8.26US$ and 5.12US$. However, the cost was higher than the mean cost of drugs observed previously (9) among pediatric inpatients who are less likely to suffer from multiple diseases. The cost of the prescription (and treatment) is an important variable in determining accessibility and concordance to treatment especially in Nepal where the per capita income is 260US$ per year (24). MTH is a private sector health care provider where most of the patients have to pay for their treatment and medicines. But, to make the treatment accessible to patients belonging to low socioeconomic groups, the Poor Patient Fund (PPF) has been created and MTH organizes free treatment service 'camps' outside the hospital. These are health check up programs conducted by the hospital in outside locations. These could either be within Pokhara city, within the valley or outside

IAMs were prescribed in 57% of the patients. In a study from western Nepal (12), 51% of the patients were prescribed injectable antibiotics. In an Indian study (25), 42.5% of patients were prescribed antibiotics parenterally. Similarly, in an Israeli study (26), 64% of patients were prescribed antibiotics parenterally. Apart from the cost associated with the injection procedure, IAMs are themselves costly. Early

switch over from IAMs to oral antimicrobials can decrease the financial burden. An implementation program promoting early switch over from intravenous to oral quinolones ensured a total hospital saving of 41420US$ during the time period considered (27). Similar programs could be implemented in MTH for cost effective use of IDs/IVFs.

Ampicillin and Cloxacillin FDC was defined to be irrational by the Drug and Therapeutics Committee of MTH and was not available in the MTH pharmacy. But, still a few prescriptions contained FDC. Coamoxiclav was the most commonly prescribed injectable FDC anti-microbial. Furthermore, it was found that a combination of three anti-microbials (betalactam, aminoglycoside and metronidazole) was often prescribed to patients. Educational interventions to reduce the prescription of coamoxiclav are underway and managerial interventions are being planned. The process of framing a hospital formulary is also in progress.

Departmental comparison showed the average number of IAMs prescribed was highest in OBG followed by Surgery, Pediatrics and Medicine. The lower mean does not signify that prescription of anti-microbials is lowest in Medicine because anti-microbials might have been used orally. Generally, prophylactic antibiotics were given parenterally in OBG and Surgery and that might be one of the reasons for the higher mean number of IAMs in these departments.

To prevent injection-associated infections, injection use needs to decrease and injection safety must be achieved (28). Several interventions were conducted world wide to decrease injection overuse and/or to achieve safer practice (28,29). Some of them were very successful. Better communication between prescriber and patients and managerial approaches (i.e. restricting access to selected unnecessary and dangerous injectable drugs) can reduce overuse (28). The authors of a study conducted among private sector injection providers (pharmacies/medical shops and other venues) in the central region of Nepal (30) found unnecessary and unsafe use of injections to be common. Adverse effects like abscesses were common, unsafe handling and disposal of injection equipment and sharps is common and reuse of non-sterile injection equipment with the same patient was commonly observed. Providers failed to wash their hands or take other precautions while injecting and recycling waste was a problem (30). Certain of the problems mentioned may also be applicable to the hospital setting.

Parameters	**Department**			
	Medicine	**OBG**	**Pediatrics**	**Surgery**
Duration (days)	7.89 (6.34)	5.57 (4.43)	5.53 (3.82)	6.65 (6.04)
Number of drugs	9.56 (5.13)	10.60 (4.72)	5.43 (3.77)	9.86 (5.64)
Number of injections	3.89 (3.08)	7.14 (4.21)	3.08 (2.78)	6.58 (3.94)
	Frequency (percentage of total prescriptions for IAMs in the particular department)			
	(N=104)	**(N=72)**	**(N=103)**	**(N=154)**
No. of IAMs				
1	50 (48.08)	18 (25.00)	53 (51.46)	67 (43.51)
2	37 (35.58)	20 (27.78)	31 (30.10)	44 (28.57)
≥ 3	17 (16.34)	34 (47.22)	19 (18.44)	43 (27.92)
	Frequency (percentage of total prescriptions for IVFs in the particular department)			
	(N=184)	**(N=81)**	**(N=89)**	**(N=163)**
Intravenous fluids				
Dextrose Normal Saline (DNS)	122 (66.3)	38 (46.91)	4 (4.49)	114 (69.94)
Ringer Lactate (RL)	27 (14.67)	76 (93.83)	12 (13.48)	136 (83.44)
Normal Saline (NS)	101(54.89)	12 (14.81)	6 (6.74)	93 (57.06)
5% Dextrose	20 (10.87)	37 (45.68)	0 (0)	42 (25.77)
10% Dextrose	15 (8.15)	1(1.23)	52 (58.43)	7 (4.29)
Isolyte P	0 (0)	0 (0)	67 (75.28)	8 (4.91)
Others	21(11.47)	1(1.23)	2 (2.25)	19 (11.66)

Table 4: Comparison of various parameters, frequency of injectable antimicrobial (IAM) use and use of intravenous fluids (IVFs) among four major departments of MTH

In the West, the need for parenteral therapy is an indication for hospitalization. Patients managed with other agents are treated as outpatients saving money for the healthcare system. In Nepal, patient demand for injections, and the inappropriate use of injections are a common health problem (31). Parenteral therapy is often started and maintained for the satisfaction of the patient, because of the patients' expectations of quicker recovery and for satisfying patient demand (*Personal observation of the authors*). So the issue of parenteral drug treatment in Nepalese hospitals should be studied in more detail.

Our study had many limitations. The study describes the pattern of injectable utilization, but did not investigate the reasons why. The study was carried out over a six month period (during the winter and summer months) and seasonal variations in disease pattern and drug utilization were not considered. A study of one year duration can offset the effect of seasonal variations. Drugs used for induction and maintenance of anesthesia, which are generally more expensive than drugs for many other uses, were also not considered but this was due to lack of proper documentation. Only the drug costs were considered and other costs were not taken into consideration. We did not look for the frequency of needle stick injuries among health workers. Follow-up of the patients and their opinion regarding the injectable use was not done and the rationality of drug use in different conditions was not assessed.

CONCLUSION:

The study provides an overview about utilization of IDs/IVFs among inpatients in MTH and could serve as a basis for further research, which will help prescribers to improve patient management by rationalizing injection practices. The high rate of prescription of IDs/IVFs is a matter of concern. Decreasing the prescription and early switch over to oral preparations will significantly reduce both the drug and non-drug cost (cost of injection, surgical items and hospital & nursing charges). Guidelines for the prescription of injectable drugs (including IAMs) are required.

ACKNOWLEDGEMENTS

We acknowledge the help of Mr. Resham Thapa of the Medical Record Department (MRD), MTH and other staff of the department in carrying out the study. The help of Mr. Arjun Shrestha and his team of the Central Library, MCOMS, in searching relevant literature for the study is also gratefully acknowledged.

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CASE REPORT

Total revision of the hip using allograft to correct particle disease induced osteolysis: A case study

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ABSTRACT: Total hip replacement is considered to be a highly successful and routine surgery; however, the internal components produce particles through friction and wear in the device. These particles are identified as one of the main reasons for total hip revisions. The generated, biologically active, particles provoke the formation of osteolytic areas through the inhibition of bone formation and increased fluid production. The resulting bone loss can be managed through the use of allograft bone in combination with bone chips and cement. In addition, implants constructed with highly porous trabecular metal can be used to further facilitate rapid and extensive tissue infiltration resulting in strong implant attachment. In this case study we show the use of a tibial allograft coupled with bone chips and cement to cover and support a lytic cyst in the proximal femur, distal to the greater trochanter. Additionally, we detail the use of a trabecular metal cup to halt the migration of the component into the acetabulum and promote greater fixation and bone ingrowth.

KEYWORDS: Revision Hip Arthroplasty, Allograft, Osteolysis, Particle Disease, Trabecular Metal

INTRODUCTION

Total hip replacement is considered to be a highly successful and routine surgery. It is estimated that over a million such medical procedures occur annually world-wide. However, despite the minimal rate of early complications, up to 30% of all surgeries are revised within 10-14 years of initial surgery (1). Every prosthetic hip replacement available produces particles. These particles are identified as one of the main causal reasons for total hip arthroplasty. The wear between primary binding surfaces of the femoral head and acetabular components in total hip replacements is considered to be the most significant source of prosthetic particles (2).

One estimation, from a study utilizing a metal on polyethylene joint, suggested the generation of hundreds of thousands of polyethylene particles during each gait cycle (3). Another study found that metal-on-metal or ceramic-on-ceramic pairings had significantly less wear on the prosthesis (4). However, despite the variances in particle generation of different materials, osteolysis is indicated in all types of hip replacements. Strictly defined, osteolysis refers to an aggressive local bone resorbtion. Particle debris generated from the mechanical wear of prosthetic devices is known to alter the function of multiple cell types in the periprosthetic area, including macrophages, fibroblasts, osteoblasts, and osteoclasts (5-7). The generated biologically active particles appear to provoke the formation of lytic areas through the inhibition of bone formation and increased fluid production (8-10). These cysts ultimately lead to implant loosening.

Bones are highly dynamic tissues undergoing a constant remodeling process that is regulated by a tightly-controlled balance of osteoblast and osteoclast activity. The major challenge of revision hip arthroplasty is related to osteolysis and bone loss decreasing stability of the implant. Revision of the acetabular component can be especially challenging because of deficient bone stock. The loss of bone can surmount due to surgical bone loss from the primary operation, migration of the cup, and as mentioned previously, particle induced osteolysis (11). Consequently, the goal of revision hip surgery should be anatomical placement of the acetabular component, but

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this can be difficult to achieve in cases where contact between host bone and the implant is diminished. This bone loss can be managed by either filling the absent area with cement, the use of allograft bone, or by using special implants such as those constructed with trabecular metal (12-16). Allograft incorporation can be implemented to reinforce the lytic area, thereby stabilizing the implant. Allografts do not suffer from osteoclastic invasion and it has been shown that osteoblasts deposit osteoid across the host bone and the dead graft (17). This union results in an increased mechanical resistance that is indicated by increased radiological density throughout the graft (18).

The structure of trabecular metal resembles bone and approximates its physical and mechanical properties more closely than other prosthetic materials. The highly porous trabecular configuration is conducive to bone ingrowth, facilitating rapid and extensive tissue infiltration resulting in strong implant attachment (19). Trabecular metal consists of interconnecting pores resulting in a crystalline micro-textured biomaterial that is 80% porous. This allows for greater tissue ingrowth (2-3 fold higher compared to conventional porous coatings) with approximately double the interface shear strength (19). In hip arthroplasties, porous trabecular metal facilitates bone ingrowth and fixation of the device; multiple studies have shown that most replacements can be reconstructed with an uncemented trabecular hemispherical cup with screws with or without morselized bone graft (20-22). Because of their porous surface and mechanical properties trabecular metal cups provide a promising approach for offering a better environment for bone graft remodeling (23). In this case study we detail the use of a trabecular metal cup to halt the migration of the component into the acetabulum and promote greater fixation and bone ingrowth. Additionally, we show the use of a tibial allograft coupled with bone chips and cement to cover and support a lytic cyst in the proximal femur, distal to the greater trochanter.

CASE STUDY

A 73 year old man presented with instability in the left hip, 17 years after bilateral hip arthroplasty was completed. The original replacement was a ceramic head on a polyethylene lined acetabular component. Still working full time and an active individual, instability and loss of control began to impede on his daily activities. Sharp pain presented down the lateral aspect of his left leg during jarring actions. During physical examination, good range of motion and gait was displayed in both hips, although pain was produced during forced external rotation of the left hip. Leg length was equal.

X-rays showed significant osteolysis of the proximal femur, distal to the greater trochanter of his left hip (Figure 1). Despite the bone loss, the stem appeared to still be solid. In addition, significant wear of the left cup was observed. It was anticipated that the progressive wear of the polyethylene cup would induce small particle disease involving the greater and lesser trochanter areas. X-rays had been taken 5 years prior to evaluate the aging arthroplasty. Comparison to the current x-rays (Figure 1) revealed that the particle disease had expanded and significantly increased the endosteal lytic zone, it was also evident that the ceramic head had penetrated deeper into the acetabulum. The right hip was not radiologically or symptomatically threatened at the presented time. To avoid impending femoral fracture or avulsion of the greater trochanter from lytic bone loss, revision of the left hip was scheduled.

OPERATIVE TECHNIQUE

Since the stem had good fixation, the choice was made to leave it in place and use a bone graft to support the lucent area distal to the greater trochanter. A tibial allograft was used to secure the femoral component and stabilize the lytic area. The allograft was irradiated with 2.5 Mrad (25,000 Gy) in the hospital bone bank, accrediated by the American Association of Tissue Banks, and consequently stored at -70 degrees Celsius. The approximate allograft size was templated preoperatively and a longer graft ordered to account for any intraoperative adjustments. The allograft was only brought into the operating room after possible infection of the to-be-revised hip was ruled out. In order to reduce operative time, the allograft was prepared on a separate table by members of the surgical team while the

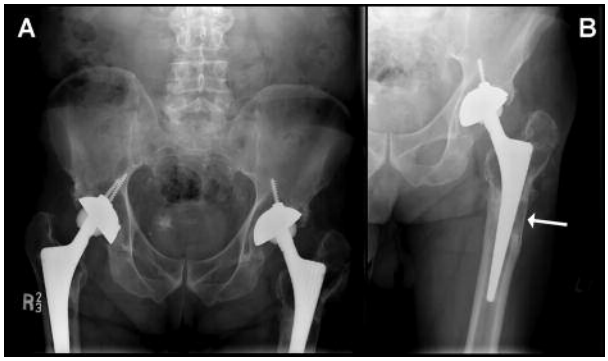

Figure 1: Pre-operative X-rays in the coronal plane. Lucency in the lesser and greater trochanter is evident with the endosteal lytic area marked by a white arrow. It is also apparent that the left acetabular component has pushed deeper into the acetabulum.

revision was initiated. The femoral component had good fixation so additional bone ingrowth was not a major concern. Thus, cement was used to fill in the lytic area and provide additional structural support. Polymethylmethacrylate bone cement has been known to strengthen allograft bone, impair resorbtion, and allow for the delivery of antibiotics (24). Cement was not used between the allograft and the host bone, only in the lytic area between the allograft and the implant, so as not to impair healing at the host-donor interface. Additionally, morselized bone from the allograft was used between contact sites of host and donor bone in an effort to increase bone ingrowth. Finally wire was used to secure the allograft to the femur.

Operative visualization confirmed the cup had protruded into the acetabulum and wear on the polyethylene lining was evident, necessitating its replacement. A Zimmer Trilogy™ Acetabular System was selected to replace the acetabular component, consisting of a metal shell, polyethylene liner, and screws. The shell, made from Tivanium™ Ti-6Al-4V alloy, is pourous to allow for fixation with Tivanium™ alloy cortical screws. In this case, three 6.5mm screws of lengths 25, 30, and 35mm were used to secure the cup into the acetabulum. The original cup was uncemented, 56mm in size and was replaced with a similar 56mm trabecular metal cup. The porous trabecular metal serves to facilitate bone ingrowth and increased fixation of the arthrography. Bone chips from the excess allograft were also used to fill in the protruded acetabulum from the original implant. This will further stimulate bone growth in and around the new trabecular component.

DISCUSSION

Immediately following the surgery the patient was taken to radiology for post-operative x-rays (Figure 2). Revision of the acetabular component with a trabecular metal cup was then visualized and correct placement within the acetabulum was confirmed. The original femoral component was also visualized, shown reinforced with a well placed tibial allograft.

Post-operative management of the revision hip replacement includes a diligent rehabilitation program. Revision cases are usually rehabilitated more conservatively than primary replacements, as was the case here. This patient was treated with additional care due to the use of allograft bone to stabilize the femoral component. During the first week post-op, progressive ambulation remains the primary goal. Our patient was encouraged to begin range-of-motion ankle exercises and moving with a walker/assistance 5 to 10 feet the first day after surgery which was done with success. Throughout the first week, aided walking was extended to 25-45 feet and stair-climbing with crutches was introduced after day 5. Stair climbing and other motions that bend the knee must be watched carefully as for the first 3 months the patient is advised not to bend their knee past 90 degrees. This helps to avoid dislocation and damage to the hip and device. The patient progressed very well through the rehabilitation program as proposed.

Additional x-rays were taken after 3 months to confirm fixation of the aetabular component and evaluate the success of the tibial allograft over the osteolytic area in the proximal femur (Figure 3). The acetabular component appeared to be well placed and the observed migration into the acetabulum was halted. The tibial allograft, marked with a white arrow, remains in place supporting the area of osteolysis. The level of

Figure 2: X-ray of the left hip after surgery. Revision of the acetabular component with a trabecular metal cup is marked with a black arrow. The original femoral component is shown reinforced with a tibial allograft, marked by a white arrow.

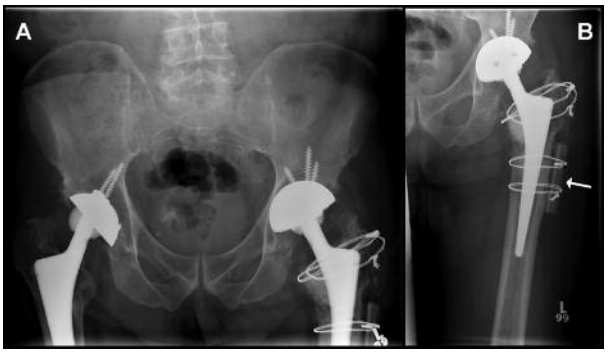

Figure 3: Coronal X-rays taken 3 months post-operatively. The acetabular component appears to be well placed and the progressive push into the acetabulum appears to be corrected. The tibial allograft, marked with a white arrow, remains in place supporting the area of osteolysis. The level of transparency has reduced significantly after cleaning out the cyst and filling the lytic zone with biocompatible cement.

transparency had reduced significantly after successful cleaning of the cyst and filling the lytic zone with biocompatible polymethylmethacrylate bone cement. Physical examination was completed at the same time as x-rays to ensure the patient had continued with the rehabilitation program and was continuing to make significant progress. Ambulation, range of motion, and functionality were all observed and were progressing well. The patient is now fully recovered, ambulating and functioning without pain or discomfort.

For reasons including particle disease, revision of total hip replacements generally occur upon indication of a painful loose prosthesis. Davis et al. (25) used the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) questionnaire to grade pain and function pre- and 2-year-postoperatively. The study reported that a higher pain level and number of comorbidities before the surgery predicted poorer outcomes at 24 month post-surgical follow-up. Patients with better preoperative WOMAC pain and function scores had better scores postoperatively, suggesting the benefit of performing total hip revision not only to relieve current symptoms, but to reduce the chance that pain and function will worsen while waiting for surgery. In this case, loosening was first noticed by the patient through instability and loss of gait control and later confirmed through radiography. If surgery had waited until higher levels of pain were expressed to maximize the life of the original device, more serious complications may have occurred. By performing the revision more complicated surgeries with worse outcomes, potentially for failure due to fracture, are avoided. The use of allograft is shown as an effective way to support components threatened with osteolysis. Donor bone in combination with biocompatible cement can greatly reduce the potential for injury and pain due to lytic bone loss.

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CASE REPORT

Morgagni hernia: Ten years of idiopathic vomiting

Ahmed A. Mustafa Khalil* and Aim M. McMillan

INTRODUCTION

Morgagni hernia was first described in 1769 by the Italian anatomist Morgagni (1). This hernia is a rare congenital diaphragmatic hernia comprising 2-3% of all diaphragmatic hernias (1, 2). The bowel, stomach, omentum or even the liver can herniate into the chest through a congenital retrosternal defect where the diaphragm joins the costal arch, as first described by Larrey, Napolean's chief surgeon (3).

A very small defect is gradually stretched with time, explaining why many cases are silent until adulthood, and presentation may vary from non-specific gastrointestinal symptoms to bowel obstruction and strangulation (2, 4). Gastric outlet obstruction is often the presenting picture when the stomach herniates into the sac (5, 6).In childhood, pneumonia is an important presentation (7, 8).More than half of patients can be diagnosed incidentally while investigating unrelated problems and most symptomatic cases tend to present acutely (9). Despite careful investigations for various presenting symptoms, diagnosis is unsuspected until incidental finding of the hernia on laparotomy or laparoscopy (9).

We report a patient who was thoroughly investigated over ten years for repeated vomiting. Repeated chest radiographs, endoscopies, oesophageal manometry and barium follow through revealed no abnormalities. Finally, a CT scan obtained to rule out chronic pancreatitis, showed the hernia and excluded pancreatitis. Subsequently, laparoscopic mesh repair allowed for rapid recovery.

METHOD

A 35 year old male presented with unsettling vomiting for seven days. He suffered attacks of vomiting and dysphagia for ten years with rapid deterioration and 12.5 kilograms weight loss in the past six months. Over the years, he was treated with different proton pump inhibitors and Metoclopromide orally with little response. The patient recognises that liquid food can improve his symptoms, and bread can aggravate his vomiting. He had a recent history of pale stool for three month that was difficult to flush as well as heavy alcohol consumption for several years.

His past medical history includes depression, asthma, latex allergy, right inguinal hernia repair when he was 12 years old and persistent vomiting for 10 years following main meals, no haematemesis, and weight loss in the past six months.

His full blood count, urea and electrolyte, liver function test and calcium levels were within normal range. Chest radiograph reported right basal consolidation and atelectasis with loss of demarcation of the diaphragm (Figure 1).

Upper GI endoscopy revealed oesophagitis, hiatus hernia, a small oesophageal nodule at 38 cm, and a normal stomach and duodenum. Histopathology revealed an eosinophilic nodule consistent with reflux oesophagitis.

A manometric study excluded dysmotility and reported reduced tone in the lower oesophagus.

The patient had two normal upper GI endoscopies in the past on one occasion, however, an hour glass looking stomach was reported, but no obstruction was noted.

A small bowel follow through was requested to investigate steatorrhoea, revealing an unusual lie of the stomach position with a degree of malrotaion. Otherwise the examination was unremarkable (Figure 2).

A CT scan of the abdomen showed a normal pancreas, and a 5x8 cm defect in the right hemi-diaphragm representing a Morgagni hernia. The sac contains half of the stomach body, transverse colon and mesentery, with no evidence of bowel obstruction (Figures 3 and 4).

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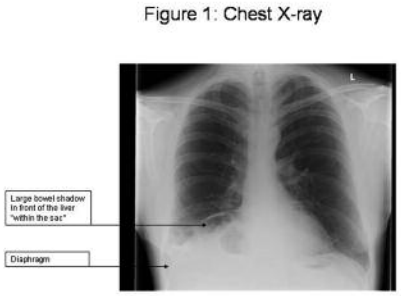

Figure 1: Chest X-ray

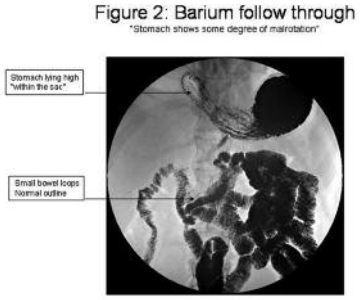

Figure 2: Barium follow through
"The stomach shows some degree of malrotation"

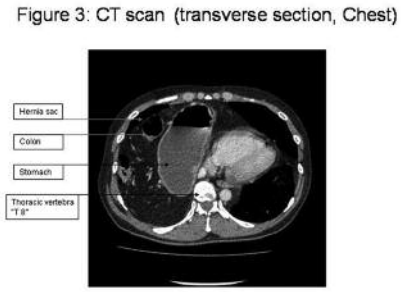

Figure 3: CT scan (transverse section, Chest)

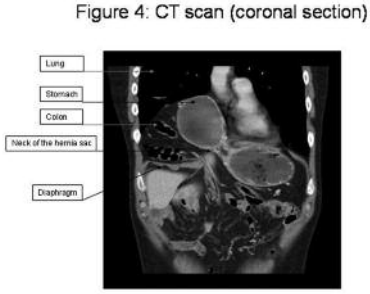

Figure 4: CT scan (coronal section)

On laparoscopy, the colon and stomach were pulled down with ease from a wide sac that extended to the right side of the chest. Laparoscopic excision of the sac was performed by dissecting the plane between the peritoneal sac and the pleura which easily pealed off. The diaphragmatic defect was repaired with a 10x15 cm composite mesh (Bard® Composix Mesh®) and was fixed in place with Auto Suture (ProTackTM).

DISCUSSION

Although the bulk of reports confirm that Morgagni hernia often remains silent and the majority of cases are discovered incidentally while investigating unrelated problems, the majority of symptomatic cases present acutely with potentially life threatening obstruction and strangulation (9). Pallati et al presented a case of gastric outlet obstruction, diagnosed as Morgagni hernia involving the stomach at laparotomy (5).

Lateral view chest radiographs can be helpful and may show an anterior mediastinal mass typically to the right of the midline. Iso et al presented a case of acute intestinal obstruction with air fluid level in the chest and right side of the chest on plain X-rays of the abdomen and chest (10). In children, it might only show features of consolidation. However, the diagnosis can be missed (7) and in the patient in this case presentation, the chest radiograph did not raise a suspicion of a diagnosis of Morgagni hernia.

Contrast studies can be completely normal (9) and usually depend on whether any bowel or stomach herniates at the time of the study. This was the case in the patient presented in this case report, and a barium follow through was not helpful in the diagnosis.

Nearly all cases of gastric outlet obstruction will necessitate an upper GI endoscopy. However, in the patient in this case report, endoscopy was not conclusive on three occasions. This may reflect either intermittent herniation or reduction of the stomach while inflating or inserting the endoscope. Dodis et al reported that endoscopy was also inconclusive in his case report (11).

Although this patient was symptomatic for ten years a CT scan and operative findings confirmed the presence of a large hernia with colon and stomach content, all other investigations had been unsuccessful. This case demonstrates the difficulty of diagnosing patients with a Morgagni hernia. While many cases have been diagnosed on chest radiographs and CT scans, the patient presented in this report remained undiagnosed until a CT scan was requested to rule out another

diagnosis. The CT scan demonstrated both the extent and contents of the hernia and identified its anatomical location. Thus a CT scan is the diagnostic method of choice and can confirm up to 100% of cases, it can differentiate the hernia from other mediastinal masses and chest pathologies as well as provide a detailed description of the diaphragmatic defect and hernia sac, including its contents (12-14).

The defect is usually small and situated to one side of the midline (2, 15). It is likely that this patient had an intermittent herniation through the unusually wide neck with strangulation and initiated repeated episodes of gastric outlet obstruction. Furthermore, it is possible that the stomach had repeatedly been reduced back into the abdomen before diagnostic imaging was performed. The most recent presentation, which prompted the diagnosis, may have reflected an attack of incomplete gastric volvulus that led to intense vomiting and dysphagia.

CONCLUSION

Morgagni hernia is a rare diaphragmatic hernia. It is usually asymptomatic, but can present with a non-specific symptoms, posing a challenge to its diagnosis. Patients with long-standing symptoms of gastric outlet obstruction and negative routine radiographs and endoscopy, should be suspected for a diagnosis of Morgagni hernia. Early CT scan should be considered as it is both sensitive and specific.

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CASE REPORT

Jejunal Intussusception as an Unusual Cause of Abdominal Pain in an Adult

Rohtesh S. Mehta

INTRODUCTION

Intussusception is a relatively common etiology of abdominal pain in pediatric population and is usually idiopathic. In adults, on the other hand, this entity is seen infrequently and a lead point can be recognized in a vast majority of cases. This is a description of a case of a young male who presented to our hospital with abdominal pain and was diagnosed with jejunal intussusception without any obvious underlying cause.

CASE

A 29 year-old white male with past medical history significant for hepatitis C, factor V leiden deficiency, femoral-popliteal bypass surgeries twice for arterial clots, and anxiety disorder presented to the emergency department with a chief complaint of peri-umbilical abdominal pain. He described the pain as moderately severe and colicky in nature, intermittent, radiating from right upper quadrant to the left. The pain started a week pior, preceded by nausea, vomiting and diarrhea, and had been progressively getting worse. He had two to three episodes of vomiting and liquidy diarrhea per day. He did not notice any blood in his vomit or stools, and there was no association of the pain with food intake.

On review of systems, he denied any fevers, chills, weight loss, burning micturation, flank pain, recent camping or travel, or any sick contacts. He mentioned taking amoxicillin for three days after a dental procedure two weeks prior to the presentation. Further review of system was otherwise negative.

He was an active smoker with more than ten pack-year smoking history, and admitted to using intravenous drugs in the remote past. He consumed beer on weekends, and smoked marijuana occasionally. His home medications included duloxetine, diazepam and warfarin (which he stopped taking after the dental procedure). His family history was not contributory.

Physical examination demonstrated a tall, well built male. Vital signs were stable with mild tachycardia (HR 100) but no fever. He was anicteric, in mild distress secondary to pain. There was moderate tenderness in the peri-umbilical region with no rebound tenderness or guarding. Murphy's sign was negative, and there was no costovertebral tenderness. Bowel sounds were somewhat hyperactive. No organomegaly or lymphadenopathy could be appreciated. There were no noticeable dermatologial changes other than old tattoo marks on both arms. Rectal stool examination was guaiac negative. The rest of the examination was within normal limits.

Laboratory investigation revealed white cell count of 7.4 (4.5-11.0) Thou/u, hemoglobin of 16.2 (12.0-16.0) g/dL, platelets of 143 (150-450) Thou/u, sodium 137 (136-147) mmol/L, potassium 4.1 (3.5-5.0) mmol/L, chloride 101 (98-108) mmol/L, bicarbonate 28 (23-32) mmol/L, BUN 19 (9-22) mg/dL, and serum creatinine 0.9 (0.6-1.2) mg/dL. His lipase was 26, serum albumin 4.2 (3.0-5.0)g/dL, total bilirubin 1.2(0.3-1.1) mg/dL, alkaline phosphatase 46 U/L (42-157), AST 73 U/L (14-48), ALT 117 U/L (7-58). Urine drug screen tested positive for cannabinoids, otherwise urinalysis was within normal limit.

A computed tomography (CT) scan of abdomen was performed which revealed several loops of jejunum with apparent wall thickening and "targetoid" appearance with short segment intussusceptions. There was no evidence for retroperitoneal adenopathy or hematoma, and no pelvic mass or free fluid was noticed. The radiological appearance was consistent with jejunal intussusceptions of unidentified cause. (Please refer to figures 1 and 2 for CT scan images.)

He was initially managed symptomatically with intravenous normal saline fluids, NPO status and pain management. Overnight, he had minimal improvement in his symptoms and continued to have intermittent diarrhea. He subsequently underwent a radiocontrast small bowel follow-through examination after which his symptoms improved spontaneously. The study demonstrated moderate dilatation of loops of the mid jejunum in the right upper quadrant which was of uncertain etiology. There was no evidence of narrowing,

obstruction, intraluminal filling defect, inflammatory bowel disease or intussusception at that time.

His stools tested negative for leucocytes and no C difficile toxin was identified. There were no ova or parasites in stools, and the cultures grew heavy growth normal fecal flora, without any salmonella or shigella. The hepatitis panel was negative for A and B, but positive for C, consistent with his history of Hepatitis C. Additionally, the HIV test was negative.

As his symptoms had improved noticeably, he was therefore discharged home with an advice to follow-up as an out-patient with his primary care physician. The final diagnosis was 'idiopathic jejunal intussusception'.

DISCUSSION

Intussusception is the telescoping of proximal portion of bowel (called as intussusceptum) into an adjacent distal bowel (called as intussuscipiens). It is an infrequent cause of abdominal pain in adults. As opposed to that in children, most of the cases (about 90%) in adults have an identifiable cause while the rest are idiopathic. The lead point of intussusception is usually in the small intestine (enteroenteric) ranging from about 77 – 88%, in colon (colonocolic) in 6-15% and ileocecal in about 5-7% and gasteroenteric in about 2% of the cases (1, 2).

In a study of 58 cases of surgically proven adult intussusceptions, most patients were found to have presented with signs and symptoms suggestive of bowel obstruction (13). However it may present in a variety of spectrum ranging from acute to chronic symptoms such as abdominal pain, nausea and vomiting in about 80%, malena or guaiac positive stools in 29%, constipation, weight loss and fever in about 10% each, and diarrhea or abdominal mass in 7% each (13). A currant jelly stool, that is a typical presentation in children, is not usually seen in adults. These symptoms are non-specific and thus, the diagnosis depends largely upon the radiological studies and a CT scan is the most effective diagnostic modality.

Some of the reported causes of enteroenteric intussusceptions are adenomas (6), lipoma, neurofibroma (13), scleroderma (13), Peutz-Jeghers syndrome (13), malignant neoplasms (5,13), and rarely metastatic disease from neoplasms such as melanoma (7,13), lymphoma (13), hepatocellular carcinoma (8), and osteosarcoma (9); other causes include adhesions, local inflammation, Crohn's disease (10) and idiopathic. Cecal cancer (14), metastatic cancer (melanoma) and idiopathic causes such as Meckel's diverticulum (14) may contribute to ileocecal intussusception. Colocolonic intussusceptions are usually due to benign causes such as lipoma, adenoma, lymphoid hyperplasia (13), malignant colon cancers (13) local inflammation, or can be due to rare complications of Crohns disease (11) and ulcerative colitis (12). Some other etiologies include blunt abdominal trauma, percutaneous endoscopic

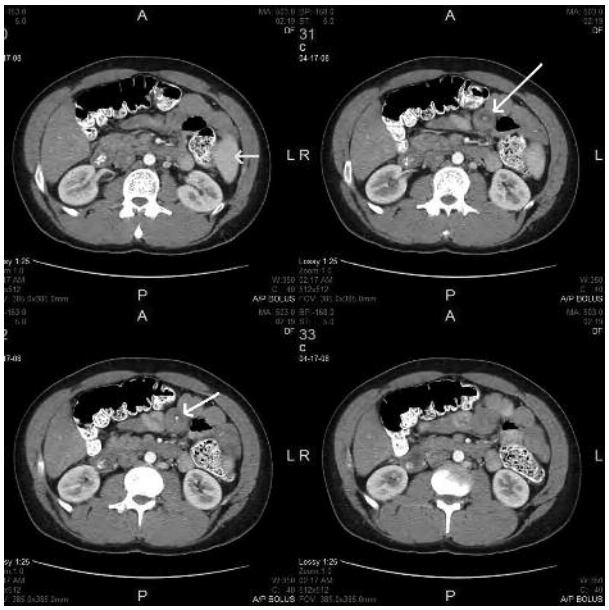

Figure 1: CT scan of abdomen demonstrating apparent bowel wall thickening (yellow arrow) within several jejunal loops in the left upper quadrant, with targetoid appearance demonstrated in several jejunal loops with associated punctate hyperdensity (white arrows image 31, 32 in Figure 1).

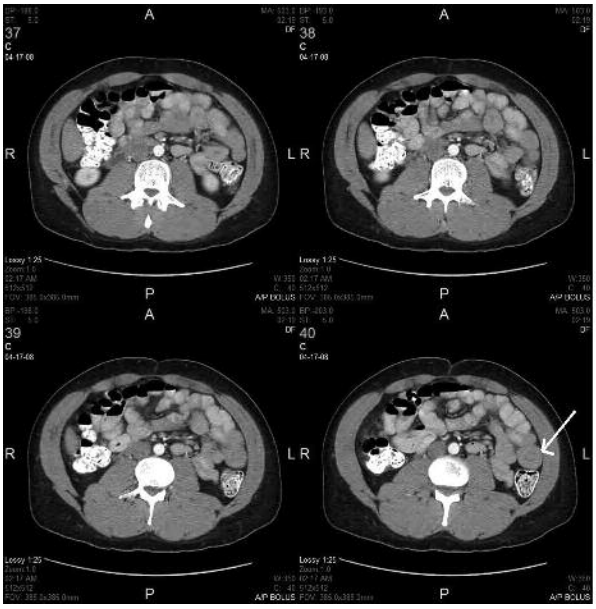

Figure 2: CT scan of abdomen with second area of targetoid appearance suggesting short segment intussusceptions (white arrow, image 40).

gastrostomy tubes, tuberculosis, systemic lupus erythematosus, celiac disease, HIV, lymphoma, and Meckel's diverticulum (2). Ascaris has also been reported as a cause of intestinal intussusception (4). Asymptomatic transient adult intussusceptions have been described in literature, which are regarded as a consequence of physiological peristalsis. These may become symptomatic when spontaneous reduction is unsuccessful (2). In surgically proven cases of adult intussusceptions, malignant causes have been described in 48% and 43% of enteric and colonic lesions respectively (13).

Most authors believed that laparotomy should be performed on all patients because of high likelihood of identifying a pathologic lesion; however, there are no universally accepted guidelines (3). As a general rule, as malignant etiologies predominate large bowel intussusceptions, resection without reduction is recommended to avoid perforation and spillage of bacteria and possible malignant cells. Small bowel intussusceptions, on the other hand, can be managed conservatively in most cases with reduction and a meticulous follow-up without the need for surgery. Nonetheless, if malignancy is suspected or the bowel is inflamed or ischemic, resection without reduction should be performed (1).

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REVIEW ARTICLE

An Unidentified Monster in the Bed – Assessing Nocturnal Asthma in Children

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ABSTRACT: Nocturnal asthma (NA) is increasing in prevalence, affecting millions of people worldwide. In addition to being associated with increased mortality, NA is associated with a decreased quality of life. NA associated sleep disturbances and increased daytime sleepiness are especially important in children due to the accompanying behavioral and developmental difficulties. As diurnal spirometry is not a practical tool for the diagnosis and monitoring of NA, self or parental reports are used. Children underreport and underestimate their NA symptoms and parents are not fully aware of their child's NA indicators. In addition, there is the lack of physician familiarity regarding the assessment and treatment of NA. Therefore, NA is chronically underreported. The development of a non-invasive, objective, home-based diagnostic tool is crucial in diagnosing and monitoring children with NA. The presence of wheeze during sleep has been successfully employed as a tool to measure NA in children. This review discusses the increasing prevalence of NA, current diagnostic tools and the consequences of undiagnosed NA in children. In conclusion, this paper suggests that an automated wheeze detective device is an objective and practical tool to aid the diagnosis and monitoring of NA.

KEYWORDS: Nocturnal asthma, Sleep disturbances, Children, Wheeze

INTRODUCTION

Approximately 300 million people worldwide suffer from asthma with the prevalence increasing by 50% each decade (1). In children, asthma is the most common chronic illness worldwide (2). Nocturnal asthma (NA) is defined as any nighttime worsening of reversible airway disease associated with an increase in symptoms and airway responsiveness (3). NA symptoms, such as awakenings, cough, wheeze and dyspnea were reported in 47–75% of asthma patients in a number of extensive surveys from different countries (4-6). Objectively, NA is defined as a diurnal reduction in forced expiratory volume in one second (FEV1) of greater than 15% (7). However, as will be discussed in this review, acquiring diurnal spirometric data for the diagnosis and management of NA is difficult, time-consuming and expensive. Therefore, NA is usually identified and monitored by nocturnal symptoms, increased nighttime asthma medication and daytime sequela.

SOURCES OF NOCTURNAL ASTHMA

A specific cause of NA has not yet been clearly defined. NA has the characteristics of a circadian disorder, a sleep-related induction of asthma and a more severe form of asthma. While everyone experiences a circadian-based nadir in lung function in the early morning, patients with NA experience a greater than normal diurnal decrease in airway function independent of sleep. The three main features of asthma - airway obstruction, inflammation and bronchial hyper-responsiveness - are all linked to a circadian nadir at 4 am (8, 9). This suggests the influence of circadian rhythms causing the nocturnal impairment of lung function (10). In addition, sleep can exacerbate lung function aggravation (11, 12). Confounding factors associated with sleep, such as the supine position of sleep and sleep-related disorders - i.e. Gastro-esophageal Reflux Disease (GERD) or Obstructive Sleep Apnea (OSA) - worsen the lung function of asthmatics during sleep and hinder the determination of

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the role of sleep in NA (13-17). Increased asthma severity does correlate with a greater risk of NA, but NA is not dependent on severe asthma (18-20). Interestingly, a specific polymorphism of the □2-adrenergic receptor has been linked with NA, but not with more severe asthma, indicating the role of genetics in NA (21, 22). The mechanism of this polymorphism's correlation to NA has not been elucidated (22, 23). Additionally, exogenous triggers such as allergens and non-allergic stimuli may provoke NA.The origin of NA is not yet known; however it is likely multi-factorial and based on the patient's unique genetic, physical and environmental characteristics.

LINK TO MORTALITY

NA is linked to an increased risk of mortality, with 70% of deaths and 80% of respiratory arrests caused by asthma occurring during nocturnal hours (24, 25). A large nocturnal variation in peak expiratory flow (PEF), as observed in NA, is not correlated with asthma severity. However, it is an independent risk factor for respiratory arrest (24). This demonstrates that NA, independent of asthma severity, is correlated with asthma-related mortality. In a 7-year follow up study of Italian young adults with asthma, NA symptoms such as nocturnal dyspnea and nocturnal tightness were correlated with a two-fold increase in subsequent overall mortality (26). Additionally, a Canadian case-control study demonstrated an increased risk of mortality for asthmatics with nocturnal symptoms (27). NA patients have been found to have 5-to-6 times more risk of accidental death than the general population, which may be attributed to nocturnal symptoms interfering with their daytime attentiveness (26). In addition, nocturnal oxygen disruptions resulting from NA lead to an increased production of potentially dangerous free radicals (28). Therefore NA must be treated as a serious chronic disorder as it is correlated to an increased rate of mortality.

INCREASING PREVALENCE OF ASTHMA

Asthma has been increasing worldwide and based on the increase of two correlating factors, obesity and old-age, it is likely to continue increasing (29-31). Obesity has been shown to be associated with an increased risk of asthma in both children and adults (32, 33). As the incidence of obesity in children and adults rises, asthma rates are expected to increase (34, 35). Additionally, NA has been reported to be more prevalent in the elderly (36). The percentage of the elderly population worldwide is expected to continue to rise in the coming years as the baby boomer generation ages and medical advances allow for longer lives (37). Moreover, an increase in childhood asthma symptoms has been observed in recent years and is expected to continue (38, 39). In accordance, Garner and Kohen found an increasing incidence of childhood asthma in Canadian children aged 0-5 and 10-11 (40). Whether this increased prevalence is based on an improvement in a physician's ability to diagnose asthma or a rise in the causes of asthma is unknown. It is important to consider the vast majority of information on asthma prevalence in children comes from epidemiological studies involving school-based surveys. In developing countries this would institute a sampling bias as many children from lower-income families do not attend school or go home early to help provide for the family. Compounding this, socioeconomic status is negatively correlated with asthma severity and nocturnal symptoms (41). Thus, the rates of asthma may be higher than reported in developing countries. As the number of asthmatics rise, tools for effective diagnosis and monitoring of NA symptoms will become increasingly vital.

UNIQUE MECHANISM OF NOCTURNAL ASTHMA

Diurnal FEV1 is an objective test for NA, though it does not account for subjective symptoms. Morgan et al. reported that the FEV1 of NA patients was on average 31% lower in the early morning than in the previous afternoon, but no detectable changes in the respiratory rate or expiratory duration were found during sleep (42). This demonstrates that the NA patient may not take action during sleep to compensate for a lack of oxygen. This can lead the asthmatic to undergo intermittent or acute hypoxia which can increase the levels of reactive oxygen species (ROS) leading to pathological effects (28, 43). Additionally, nocturnal asthmatics do not undergo the normal asthmatic adaptive response of increasing lung volume to combat increased airway resistance and maintain airway patency (44). This relationship does occur in asthmatics without NA and in non-asthmatics, indicating a unique mechanism of bronchoconstriction in NA (44).

DIURNAL SPIROMETRY TO ASSESS NOCTURNAL ASTHMA

The gold standard for the identification of asthma is clinical history, physical examination and laboratory spirometry with challenge testing. Spirometry demands a skilled technician to guide technique and interpret results. It is impractical for a technician to collect the required nighttime and morning spirometric data to accurately assess NA. To overcome this problem, the European Respiratory Society recommended day-to-day home spirometry for child asthmatics to measure

variation in pulmonary function (45). Initially, mechanical meters were used and the patient was instructed to fill out a diurnal PEF diary. However, it was demonstrated that written PEF diaries were unreliable (46, 47). Electronic home spirometry devices that automatically record data were employed to combat this issue. However, the spirometric data had poor concordance with other parameters of asthma severity and thus was deemed not clinically useful (48). Additionally, home spirometry compliance and test performance varies greatly in children, providing a biased picture of changes in lung function (49). Home spirometry is also impractical for children, as it requires extensive training and follow-up to ensure proper testing technique (50). At present, there is no practical way to collect a child asthmatic's diurnal spirometric data.

SELF AND PARENTAL QUESTIONNAIRES TO ASSESS NOCTURNAL ASTHMA

The simplest and most common method of assessing NA is self-completed questionnaires. Self-identification of NA symptoms is very difficult since the patient must clearly understand the meaning of the questions posed towards them regarding wheezing, coughing and sleep disturbances and be conscious of their nighttime symptoms (51). Falconer et al. found that adults have poor agreement between subjective self-estimation and objective measurements of nocturnal cough, a common symptom of NA (52). Physicians are often unaware of their patients' NA symptoms as patients generally have an indifferent view of NA symptoms and do not regularly report them to their doctor (53). In their study of 13,493 asthmatics, Raherison et al. found that only 48% had agreement between their actual NA situation and what was recorded by their general practitioner (6). Moreover, 42% of patients who declared they had no nocturnal symptoms had NA according to objective tests (6). This demonstrates a striking inability of the patient and the doctor to declare and identify NA symptoms. Identification of NA is vital as patients with NA symptoms have the lowest awareness of inadequate asthma control (54). Children have more difficulty in self-diagnosing NA than adults, as they are generally less aware of indicators (55). Physicians must be aware of this and specifically question asthma patients, especially children, regarding their NA status.

For children, parental reports/questionnaires are often employed in addition to self-diagnosis (51). Cultural and educational conditions play an important role in the answering of these questionnaires (56, 57). Parents must understand the terms used to describe NA symptoms and literacy is required to complete questionnaires. Parents often do not know when their child falls asleep, are unaware of most awakenings and are not able to identify nighttime wheeze (58). Less than 40% of parents with a child who is asthmatic report their child's NA symptoms appropriately (18). Moreover, NA is more prevalent and asthma more severe in areas of low socioeconomic status, possibly due to environmental factors (41). Parents in these areas are more likely to have lower literacy rates of the national language (59). Low parental literacy correlates directly with worse care measures for children with asthma possibly due to a lack of understanding of asthma symptoms and lack of ability to report symptoms to a physician (60). As such, the risk of underdiagnosis and undertreatment of asthma was higher in children from ethnic minority groups in the inner-city and from poorer neighborhoods (61). Parents of children at higher risk of developing NA due to environmental and socioeconomic factors do not accurately report their child's asthmatic status (62).

The accuracy of self-diagnostic questionnaires to identify and monitor a child's NA status has not been confirmed. Regarding daytime symptoms, self-questionnaires in children aged 7-12 are as accurate in diagnosing asthmatics as objective tests such as bronchial hyper-responsiveness testing (63). Additionally, recent research suggests child asthmatics as young as 7 dependably report their asthmatic status (64). However, no studies have specifically researched self-diagnostic questionnaires to identify and monitor NA. Nocturnal symptoms are associated with future asthmatic severity (65). Self-diagnostic questionnaires do not predict future asthmatic episodes in children under the age of 11, suggesting that these questionnaires may not be suitable to monitor NA (66). Sleep arousals are hard to self-diagnose as the child may have trouble remembering and reporting awakenings (67, 68) . For example, Brooke et al. found poor agreement between recorded and recalled nighttime coughing in child asthmatics (69). In a study of students aged 10-12, 21% were not able to answer if they had nocturnal cough (70).

Generally, children report more asthma symptoms than their parents (70-73) . Mallol et al. demonstrated that adolescents report higher symptoms of asthma, rhinitis, and eczema related symptoms than parentally-completed questionnaires (51). Sleep disturbance symptoms such as cough at night and awakening with wheezing during the past 12 months were reported significantly higher by the child than the parent (51). Nocturnal cough is reported significantly more by the child than by the parent (70). This is understandable since the child is more aware of their nighttime disturbances than the parent and may not necessarily

share this information with the parent. Parents of children over the age of 11 provide little to no more asthma information than is obtained through a child's self-assessment (74).

The lack of understanding of the term 'wheeze' in children impairs accurate diagnosis and asthma control. Riedler et al. reported difficulty for adolescents in understanding the term 'wheeze' (75). The difficulty in diagnosing wheeze is not limited to children. Levy et al. demonstrated that during daytime hours parents are unable to accurately assess the severity of their child's wheezing as compared to a physician or a computerized-acoustic analysis (58). In a study of India's physicians, a substantial percentage (33%) did not identify wheeze when shown in the International Study of Asthma and Allergies in Childhood ISAAC video sequences (76). Only 47% of physicians were able to identify nocturnal wheeze. Difficulty in recognizing nocturnal wheeze demonstrates the need for a more objective tool to diagnose NA associated wheeze.

Inability to identify and communicate a child's nocturnal symptoms may lead to NA being left undiagnosed, impairing treatment and leading to negative quality of life consequences for the child. For instance, a lack of awareness of NA symptoms in stable and treated child asthmatics led to poorer sleep quality and impaired daytime activity (77). Furthermore, children with nocturnal symptoms have an increased risk for future adverse asthma events (65). Constant monitoring of NA symptoms in children is crucial in order to prevent future asthma events and protect against daytime sequela.

NOCTURNAL ASTHMA ASSESSMENT

Nocturnal asthma is monitored by a combination of clinical history, subjective self or parental questionnaires and spirometry. The use of only spirometry or clinical history consistently underestimated asthma severity in a study of children (78). As diurnal spirometry is impractical and self or parental reports may be inaccurate, NA requires a home-based objective tool to increase monitoring efficacy. This is especially important in rural and low-socioeconomic areas where overnight clinical monitoring is problematic (79). Acoustic analysis of patients while they sleep allows for a non-invasive method for diagnosing and monitoring NA.

SNORING TO ASSESS NOCTURNAL ASTHMA

Snoring is correlated with NA symptoms in children (80, 81). Snoring may cause transfer of nasal mucus to the lower airway through upper airway vibration and increased suction pressures in the pharynx. This allergen-laden mucus may induce an asthmatic episode. However, snoring is found in many more asthma patients than those with NA. Teodoescu et al. found that while 55% of adult asthmatics reported daytime sleepiness, 84% reported snoring with 38% reporting habitual snoring (82). Lu et al. reported a highly significant correlation between snoring and asthma in preschool children indicating snoring could be used as a diagnostic symptom of NA (81). However, an asthma prevalence of 28% was reported while snoring was found in 10.5% of children. This indicates that snoring may too unspecific for NA diagnosis. Studies have not confirmed a snoring parameter (length, volume) that correlates to other NA symptoms or daytime consequences (83). The results indicate snoring alone is not appropriate for the assessment of NA.

NOCTURNAL WHEEZE

Wheezing is defined as a high to low-pitched continuous musical sound judged to be of significant duration (84). Wheezing with unforced breathing is associated with the severity of airflow obstruction and thus is a good determinant for assessing asthma control (85). In addition to asthma, wheezing in children may be triggered by acute determinants such as bronchitis, bacterial tracheitis, laryngotracheobronchitis or chronic causes such as GERD, cystic fibrosis, or bronchopulmonary dysplasia (86). Children with frequent wheezing symptoms but no asthma diagnosis experience illness-related morbidity similar to diagnosed asthmatics (87). Thus nocturnal wheezing, in the absence of asthma, requires adequate identification of the underlying health issue. A lag-time of approximately two years has been reported between the first recognition of wheeze and consulting a physician for treatment (88). This indicates a lack of public awareness of nocturnal wheezing and its effects on asthmatic control and overall quality of life. Education of general practitioners and patients is required so that wheezing is not overlooked and is treated as a symptom of a possible underlying health issue.

NOCTURNAL WHEEZE TO ASSESS NOCTURNAL ASTHMA

Measurement of nocturnal wheeze has been employed as a non-invasive technique to assess NA (89, 90). Kiyokawa et al. recorded intermittent tracheal sounds in asthmatic patients and controls during sleep (91). A respiratory physician performed an auditory review and manually recorded the presence of wheezes. Although time consuming for the analyst, this method provided objective home-based information that positively correlated with subjective symptoms and inversely correlated with morning PEF. Many characteristics of

wheezes, such as amplitude, frequency range, number of simultaneous wheezes, duration and chest distribution can be recorded and measured. The parameter that best correlates with other clinical indices of asthma is total wheeze duration as a percentage of sleep (92). The use of computerized automatic acoustic monitoring devices allows for objective wheeze detection without a physician reviewing nocturnal recordings. Computerized monitoring of the percent of sleep spent in wheeze, irrespective of the respiratory phase or site, was employed as the quantitative measurement in children and produced objective results with good sensitivity (93). The same wheeze monitoring method established that the presence of wheeze correlates to less than 51% of the expected morning FEV1 and a large diurnal variation in FEV1 (94). Although not used for the diagnosis of NA, lung sound analysis with computerized analysis of wheezing and crackles was suitable for the diagnosis of bronchiolitis in infants (95). The use of computerized acoustic analysis of nocturnal wheeze is an objective, home-based method that can be used in the determination of NA and other pulmonary disorders.

SLEEP QUALITY OF NOCTURNAL ASTHMA PATIENTS

In stable diagnosed child asthmatics, knowledge of NA symptoms is required in order to properly medicate the patient and to accurately assess daytime psychological impairments which may result from poor sleep quality. Nocturnal symptoms such as wheezing, cough, sleep disturbances and daytime sleepiness are reported significantly more in stable asthmatic children with non-diagnosed NA than in non-asthmatic controls (77). Accordingly, children with well-controlled, stable asthma have poorer quality of sleep and lower morning PEF values correlating to inferior objective and subjective sleep measurement as compared to non-asthmatic matched controls (96). In children with NA there is no difference in REM latency, REM sleep, sleep latency, total sleep time, and percentage in sleep stages as compared to controls (1). This indicates that the problems are not due to sleep stage quantity but rather to sleep quality since children with NA have more sleep awakenings than non-asthmatics (77, 97, 98). This not only places strain on the child, but also on the family as awakenings are linked to a decrease in parental mood and an increase in perceived parenting hassles (99).

SIGNIFICANCE OF WHEEZE ON SLEEP QUALITY

Wheezing caused by NA correlates to an increase in the symptoms associated with disturbed sleep in both adults and children (100). Wheezing children are two times more at risk of having difficulties falling asleep and five times more likely to have restless sleep than non-wheezing children (100). In accordance, wheezing children are nearly four times more at risk of having daytime sleepiness than non-wheezing children (100). Importantly, children with nocturnal wheeze reported a higher number of nocturnal awakenings with a corresponding increase in daytime sleepiness as compared to non-wheezing controls (101). This underscores the importance of wheeze detection as a tool to monitor sleep-related behavioral problems in children.

EFFECT OF NOCTURNAL ASTHMA ON CHILDHOOD DEVELOPMENT

Children with NA report a higher incidence of disturbed sleep-associated symptoms such as vasomotor and memory deficits, depression, anxiety and daytime sleepiness (2). A study of over 100,000 children, ages 0-17, found a significant correlation between asthma and developmental, emotional, and behavioral problems (102). It can be assumed from studies documenting the rates of undiagnosed NA in the general pediatric population that a significant proportion of the population studied suffered from NA (6, 103). Further contributing to the education problems of child NA sufferers, Diette et al. noted children with awakenings due to NA had a greater number of school absences with parents having an increased number of missed work-days (104).

CONCLUSIONS

Children with NA are not suitably monitored and thus are not receiving adequate care (87). Untreated NA leads to both negative physical and developmental consequences in children. Patient-centered measures for a child's asthma control are vital for improved asthma management (105). Proper asthma control requires patients and physicians to be familiar with NA symptoms. An automated wheeze detection device allows objective measurement of an important NA symptom that is correlated to reduced morning spirometry values. A low-cost wheeze detection device to identify and monitor NA is especially important in lower socioeconomic environments where health care access is limited, asthma rates are higher and parental reports of symptoms less reliable than more affluent areas. Additionally, detection of nocturnal wheeze in children will aid in the diagnosis and monitoring of numerous other respiratory pathologies. Future studies should analyze the appropriateness and cost/benefit of nocturnal wheeze detection for NA identification and asthma control.

ACKNOWLEDGEMENTS

The author wishes to acknowledge Dr. Noam Gavriely for his encouragement in submitting this paper.

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REVIEW ARTICLE

Suppressive valacyclovir therapy to reduce genital herpes transmission: Good public health policy?

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ABSTRACT: Genital herpes is a widespread sexually transmitted infection caused by the herpes simplex viruses (HSV). Suppressive valacyclovir therapy has been shown to significantly reduce HSV transmission. The benefits and costs of using valacyclovir to reduce transmission in couples discordant for genital herpes will be analyzed in order to better inform decision-making. By reducing transmission, the physical and psychological harms of living with symptomatic genital herpes will be prevented while saving on certain healthcare costs. However, the large number needed to treat and the low symptomatic rate among infected individuals may outweigh these benefits. The costs of trying to achieve a significant reduction in incidence include the psychological harms of identifying asymptomatic individuals through a large screening program and the economic costs of the antiviral agent and screening. When these issues are weighed, the high economic costs render a program to reduce incidence unfeasible. Nevertheless, it is clinically important to consider the consequences of transmission at an individual level. The specific circumstances that influence the decision to use suppressive therapy are identified.

KEYWORDS: Valacyclovir, Herpes Genitalis, Simplexvirus, Transmission

INTRODUCTION

Genital herpes is a sexually transmitted infection prevalent throughout the world (1). Genital infections with herpes simplex virus types 1 and 2 (HSV 1 and 2) are common, but infrequently cause noticeable symptoms. The seroprevalence of HSV-2 was 9.1% in 2000 for Ontario (2) while a prevalence of 21.9% among individuals older than 12 years was reported in the United States between 1988-1994 (3). More recently (1999-2004), Xu et al. (4) reported a seroprevalence of 17.0%. A small proportion of infected individuals reported a diagnosis of genital herpes; 9.9% in 1988-1994 and 14.3% in 1999-2004 (4). Thus, most infected individuals are unaware that they are infected but are still able to spread the virus asymptomatically, serving as important transmitters of the virus.

Genital HSV-1 infections can also occur. Although HSV-1 typically causes oropharyngeal lesions and is usually transmitted by non-sexual contact during childhood (5), the virus can cause genital herpes when transmitted by vaginal or oral sex, often without visible lesions (5-8). The lesions of HSV-1 are clinically indistinguishable from those of HSV-2 (9). However, HSV-1 genital herpes infections are less severe and recur less often than HSV-2 (9-12). Howard et al. (2) found a seroprevalence of 51.1% for HSV-1 in 2000 for Ontario. Similarly in the US, HSV-1 was widespread in 1999-2004 (57.7%), but the number of HSV-1 infected individuals reporting genital herpes was 1.8% in this time period (4). HSV-1 comprises 10-15% of all genital herpes cases in the US, although regional variations exist (13). Increasing prevalence of HSV-1 genital herpes has been observed within specific populations. For instance, in an American university student population, the percentage of genital herpes due to HSV-1 increased from 30.9% in 1993 to 77.6% in 2001 (14).

The high prevalence of genital infections due to both HSV-1 and HSV-2 suggests a need to reduce the transmission of genital herpes. In 2003, the US Food and Drug Administration approved an indication for Valtrex (valacyclovir) to reduce genital herpes transmission: “Valtrex reduces the risk of heterosexual

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transmission of genital herpes to susceptible partners with healthy immune systems when used as suppressive therapy in combination with safer sex practices." (15) The same indication was approved by Health Canada in 2004 (16). Extensive marketing directed toward patients encourages them to have their HSV serostatus determined (and indirectly encourages valacyclovir use in discordant couples). Both the positive and negative aspects associated with using valacyclovir suppressive therapy to prevent transmission in couples discordant for HSV will be discussed in this paper in an attempt to better inform decision-making.

METHODS

A literature review was performed to determine the costs and benefits of suppressive valacyclovir therapy. In addition, the cost of using valacyclovir to achieve a 30% reduction in the population incidence of HSV-2 genital herpes was calculated (Table 1). Data was used from previously published articles, and all costs were converted to 2000 US dollars. For this analysis, the drug cost required for a coverage level of 30% was determined. At such a high coverage, there would be fewer outbreaks among those receiving suppressive valacyclovir. These savings were conservatively calculated by multiplying the annual cost of genital herpes by the percentage of individuals assumed to have no recurrent symptoms as a result of receiving valacyclovir suppressive therapy. This calculation assumed that all individuals receiving valacyclovir were symptomatic before treatment. Next, the lifetime savings from reducing the annual incidence of HSV-2 by 30% was calculated. The number of years required for these savings to balance the cost of the program was also determined. It was assumed that the 30% reduction in incidence occurred immediately.

Population in USA 2000 (72)	$281,421,906.00
Population with HSV-2 (17%) (4)	$47,841,724.00
30% of population with HSV-2	$14,352,517.00
Yearly drug costs per individual	$1,168.30
Drug costs at 30% coverage	$16,768,045,850.00
Yearly lifetime incident cost (51)	$1,800,000,000.00
Yearly savings from preventions	$540,000,000.00
Cost of genital herpes per year	$1,353,405,133.00
Savings due to fewer individuals seeking medical care, assuming 67% of covered individuals will have no recurrence (57)	$272,034,432.00
3 years of savings	$816,103,295.00
3 years of drug therapy	$50,304,137,550.00
Net cost	$49,488,034,255.00

Table 1. Calculating the cost (2000 US dollars) of using suppressive valacyclovir therapy to achieve a 30% reduction in the population incidence of HSV-2 genital herpes.

In addition, the cost (2000 US dollars) of preventing a single transmission of HSV-2 genital herpes by using suppressive valacyclovir therapy was calculated (Table 2). Although the number needed to treat to prevent one transmission varies among studies, the figure used in this analysis was considered a conservative estimate. The lifetime savings from preventing the single transmission was calculated using the larger lifetime cost to treat men. Further, there would again be potential savings from a reduction in symptoms among those receiving suppressive valacyclovir therapy. It should also be noted that this simplified analysis is limited since it is based on data from heterogeneous sources, each with its own methodologies and assumptions.

Number needed to treat (17)	18
Cost to prevent one transmission	$21,029.40
Savings from prevention (51)	$620
Savings from fewer outbreaks among those receiving therapy, assuming all are symptomatic (57)	$7477
Net cost per transmission prevention	$12,932

Table 2

RESULTS AND DISCUSSION

Benefits

The primary benefit of using suppressive valacyclovir therapy is to reduce transmission within discordant couples. Corey et al. (17) found that prescribing valacyclovir to individuals with symptomatic, recurrent HSV-2 infections the acquisition of genital herpes in their discordant partner was reduced from 3.6% in the placebo group to 1.9% in the valacyclovir group (hazard ratio 0.52; 95% confidence interval 0.27-0.99; P = 0.04). Since the absolute reduction was not large, the yearly number needed to treat was 38. Individuals in the valacyclovir group received 500 mg of valacyclovir once daily for eight months. This therapy effectively reduced viral shedding relative to the placebo group. As a result, it reduces transmission when the source partner does not have any recognizable symptoms but is still shedding virus, which is when most transmission events occur (18,19). The potential benefits of using suppressive valacyclovir to reduce transmissions are obvious: reducing the psychological and physical harms of acquiring genital herpes, while lowering the economic costs associated with this infection.

Psychologically, acquiring symptomatic genital herpes can have a significant emotional impact on patients (20-22). Such patients may suffer from social isolation and have difficulty initiating relationships (23,24). In contrast, other studies have shown that appropriate counseling can significantly reduce the psychological harm caused by diagnosing genital herpes (25-27). Receiving genital herpes can also cause anger towards the source partner. Additionally, the source partner may be significantly worried about transmitting genital herpes to their non-infected partner (23). Therefore by reducing transmission, valacyclovir can diminish possible psychological harms, although counseling has been shown to be effective in this regard as well (26).

Potential physical harms due to genital herpes can be prevented with suppressive therapy, assuming that the partner acquires a recognizable, symptomatic infection. Genital herpes caused by HSV-1 recurs infrequently and the frequency decreases over time with a recurrence duration of 7 days (12,28). In contrast, HSV-2 genital herpes recurs more frequently and the rate of recurrence decreases slowly over time with a recurrence duration of 8.5 - 10.1 days (28-30). Local symptoms for HSV-2 infection include pain, itching, and vaginal or urethral discharge (30). Fever, headache, and malaise occur in 39% of men and 68% of females during primary infection (30). Pain during recurrent genital herpes is reported as severe in 11% of patients, moderate in 36%, mild in 48%, and absent in 4% (21). Complications of genital herpes include dysuria, aseptic meningitis, autonomic nervous system dysfunction, transverse myelitis, yeast infections, and extragenital lesions (30).

Economically, reducing the population incidence of genital herpes will decrease such healthcare costs as hospitalizations, clinical examinations, consultations, and tests. Indirect economic costs for patients, such as time off work and traveling costs, will also be avoided (21,23,31,32). Recurrent genital herpes can also lower work effectiveness during severe symptomatic events (21). Szucs et al. (32) performed an analysis of the economic burden of genital herpes in the US for 1996. They estimated the cost of genital herpes to range from $283 million (0.1% of the US health care expenditure) to $984 million with indirect costs totaling an additional $214 million. Of the total cost, 49.7% came from drug expenditures, 47.7% from medical care (consultations and lab testing), and 2.6% from hospital costs. Szucs and colleagues (32) also calculated a cost of $60 000 per case of neonatal herpes and $2 500 for each cesarean section. In summary, reducing transmission will diminish the psychological, physical, and certain economic burdens of symptomatic genital herpes. However, it should be noted that only 14.3% of individuals with HSV-2 develop recognizable, symptomatic genital herpes (4), and as a result, the functional effect of reducing transmission on decreasing this burden is limited.

Costs

There are numerous costs associated with suppressive valacyclovir therapy in couples discordant for genital herpes. First, patients may replace safe sex practices with such therapy. Condoms offer significant, but not complete, protection against HSV-2 (33,34). Condoms also protect against other sexually transmitted infections that an individual in the relationship may have. However, Corey et al. (17) found a similar rate of condom use between the valacyclovir and placebo groups, and regardless of suppressive therapy, condom use remains low among discordant couples (19,33). It appears that suppressive valacyclovir therapy does not change couples' sexual behaviours, but further studies are required to adequately explore this relationship. Furthermore, it may be suggested that suppressive use of valacyclovir will cause antiviral resistance. Despite a lack of long-term studies, no resistance to this drug has been found for therapy lasting one year (35-37). In long-term studies with acyclovir, resistance is uncommon in immunocompromised individuals (~5%) and rare in immunocompetent individuals (38,39).

Currently, there appears to be little physical harm in taking valacyclovir every day for more than a year in healthy patients (35-37). In patients infected with human immunodeficiency virus (HIV), there are no data on the safety of therapy lasting more than 6 months (40). Headaches, nausea and vomiting, dizziness, and abdominal pain are the most commonly reported adverse effects. Psychologically, taking a drug every day may cause harm or distress. Although patients with recurrent genital herpes prefer suppressive over episodic therapy (22), it is not known how asymptomatic patients would respond to and comply with daily therapy over the long-term.

As previously described, there would be some financial savings with suppressive valacyclovir therapy, but there would also be significant economic costs associated with this program due to drug costs and screening (31,32,41). Firstly, valacyclovir costs $118.47 for 30 tablets of 500 mg, totaling $1441 a year (Canadian dollars, 2008). Another significant cost would be identifying those individuals that have an asymptomatic or unrecognized clinical infection. According to Corey (42), 60% of HSV-2 seropositive individuals have unrecognized symptoms, while 20% are subclinical (asymptomatic) with another 20% being recognized symptomatic. However all three groups have similar frequencies of asymptomatic shedding

events (19), defined as detection of HSV on the surface of skin or mucosa in the absence of genital lesions (43). Most individuals with unrecognized symptomatic genital herpes can identify their symptoms with counseling and education (42,44). Additionally, type-specific serologic tests are capable of distinguishing between HSV-1 and HSV-2 (45). The presence of antibodies to HSV-1 alone gives no information on the presence of genital herpes because the site of the infection, oral or genital, cannot be determined (26). Since HSV-1 is very common, genital herpes due to HSV-1 would be difficult to detect without swabbing genital lesions. In addition, the frequency of testing required to identify individuals with genital herpes adds to the cost of screening (45). If testing were recommended with every new sexual partner, there would be considerable strain placed on the healthcare system and the patient.

Moreover, it is predicted that there would be significant psychological harm associated with diagnosing patients with genital herpes who were previously unaware of their infection. Through a large screening program, physicians may actually cause more psychosocial harm to asymptomatic individuals, such as social isolation and reluctance to initiate relationships, than the physical harms these individuals experience (23,24,46,47). However as previously noted, studies have shown that counseling is effective in reducing psychological harm upon diagnosis (25,26). In addition, disclosing the problem to their current partner, who may raise questions of infidelity or past sexual history, may damage or ruin the relationship. Due to the additional economic cost and psychological problems of screening the general population, "it would not be useful. Screening of targeted populations, however, may be appropriate." (48) That is, a diagnosis would be more important in couples where transmission would be significantly harmful. Such circumstances may include individuals who are at increased risk of HIV infections, HIV positive patients, and patients with a partner with genital herpes (48). By diagnosing these individuals with genital herpes, infected individuals may recognize outbreaks and abstain during such periods. In fact, transmission rates may decrease after source partners disclose (49).

Cost-benefit analyses: population

Current models suggest that suppressive therapy will have a minimal effect on reducing the population incidence of genital herpes at the currently low levels of diagnosis and treatment (50). The coverage level and the duration of suppressive therapy are important factors in reducing the population incidence (50). The coverage level is primarily determined by the proportion of patients diagnosed and the proportion of diagnosed that are receiving therapy. With a coverage level of 3.2% (the current coverage in the US) and 3 years of valacyclovir therapy, it is expected that there would be a 1.8% reduction in new cases after 5 years and a 2.8% reduction after 25 years (50). The percent reduction of new cases increases to 65% with a coverage of 60% after 25 years. According to Williams et al. (50), a coverage rate of 60% is unrealistic, but they suggest that a coverage rate of 30% is theoretically possible and would reduce incidence by 30% after 25 years. Additionally, the duration of suppressive therapy can be increased. At a coverage level of 3.2%, the incidence of HSV-2 infection would be expected to decrease by 3.5% after 25 years with 5 years of therapy, compared to 1.3% with a 1-year therapy program.

The financial cost of administering suppressive valacyclovir over three years to 30% of Americans with HSV-2 genital herpes is approximately $50.3 billion (Table 1). By treating such a large number of patients with suppressive therapy, it is estimated that $816 million would be saved over the three years from reduced outbreaks among infected individuals. Thus, the net cost of a three-year program is $49.5 billion. Using the lifetime cost of an individual with genital herpes (51), the yearly savings from the 30% reduction in incidence is $540 million. Therefore, the savings from the program would balance the cost after 92 years.

Obviously, one must also consider the increased quality of life gained from a decrease in incidence. A conservative estimate of the cost to prevent one HSV-2 transmission is $12,932 (Table 2). This cost would outweigh the benefits gained since a cost of $8,200 per prevention translates to $140,000 per quality-adjusted-life-year gained, which is above the cost effective threshold of $50,000-$100,000 (52). Moreover, these calculations do not include the screening costs that would be necessary to identify asymptomatic individuals and reach the 30% coverage rate. Such screening would be essential to this program because they are the majority of individuals with genital herpes and the main group transmitting the virus (42,46). The compliance may also be lower in the general public than in the trial performed by Corey et al. (17), especially among asymptomatic or unrecognized patients (50).

Cost-benefit analyses: individual

At an individual level in Canada, the financial costs would be that of valacyclovir, $1441 each year, and the cost of screening to determine whether individuals are infected and if couples are discordant. The potential for overuse of expensive serologic testing is enormous. The psychological and physical benefits noted above may convince a symptomatic, discordant couple into asking

for valacyclovir to reduce the likelihood of transmission, but in how many instances will valacyclovir reduce transmission? Corey et al. (17) found a 48% reduction in the risk of transmission, but this reduction was from an acquisition risk of 3.6% to 1.9%. Thus, transmission is a rare event without valacyclovir use. Furthermore, when transmission does occur, most people do not develop symptomatic genital herpes. It is essential that patients understand these facts in order to make an informed decision.

Clinically, it is important to consider cases on an individual basis. Specific couple characteristics affect the significance of genital herpes transmission. These factors must be discussed before a discordant couple makes a decision regarding suppressive valacyclovir therapy. For example, prescription may depend on the HSV-1 serostatus of the partner without genital herpes. If this individual has HSV-1, they have a lower probability of developing symptomatic genital herpes upon acquiring HSV-2 (30,53-55).

In addition, the virus type (HSV-1 or HSV-2) of the source partner may be important to determine because each type causes different symptoms and has different modes of transmission. Type 1 (genital) is less likely to cause recurrent symptoms for the partner that acquires symptomatic infection (9-12). Compared to HSV-2, there is less asymptomatic shedding and, therefore, a reduced transmission rate with type 1 genital herpes (11). In addition, oral sex from a partner with a history of oral herpes is a risk factor for HSV-1 transmission (6-8,56). Transmission can occur without lesions because virus in the oropharynx can shed asymptomatically (56). Transmission from oral sex is less likely for HSV-2 because this virus is not as likely to cause an infection in the oropharynx (7,13). Moreover, the manifestation of symptoms in the HSV-2 source partner should be considered. If an individual has many recurrences each year, then it would be more feasible to prescribe suppressive therapy because the individual will receive the added benefit of reduced symptoms. However, suppressive valacyclovir therapy is not typically necessary for HSV-1 genital herpes (12,57), and the effect of valacyclovir on HSV-1 transmission has not been adequately explored. Nevertheless, valacyclovir does decrease the presence of the virus in saliva (58) and has been examined in transmission between wrestlers (59).

Another factor to consider is the duration of the infection in the source partner because infectivity likely decreases with time due to a decrease in shedding (11,33). Most infections occur within a year of contracting the virus. Wald et al. (49) found the mean number of sex acts before transmission was 40 while Mertz et al. (18) found a median number of 24. For HSV-2, asymptomatic shedding was three fold more frequent during the first three months after resolution of primary infection than after these three months (11). It is also important to discuss the number of sexual partners and the nature of the relationship. Between 1999-2004, the seroprevalence of HSV-2 was 39.9% in individuals who had 50 or more lifetime partners compared to 3.8% who had one lifetime partner (4). Transmission is most common in relationships lasting 1-6 months (49).

Transmitting genital herpes may increase the receptive partner's risk of contracting HIV in the future. The risk of acquiring HIV is approximately three times greater in HSV-2 infected men or women (60). The suggested mechanism for this interaction is likely due to the destruction of the epithelial layer by HSV-2 and attraction of CD4-positive cells (61). This relationship is important for partners that may have a higher risk of contracting HIV due to location, drug use, or sexual behaviours. Additionally, special consideration should be given to a HIV positive, HSV-2 negative partner because HSV-2 reactivation correlates with increased plasma HIV-1 levels (62,63). HSV-2 can increase morbidity and mortality for HIV infected people and may accelerate the course of HIV disease (64). HSV-2 positive, HIV-1 positive individuals may also be more efficient at transmitting HIV than HSV-2 negative individuals (64). Thus, it is important to prevent transmission of HSV-2 to HIV positive individuals (65,66). The interaction between HSV-1 and HIV has yet to be adequately explored (67).

Couples involving a HSV-negative pregnant woman and a HSV positive partner should be made aware that vertical transmission (genital HSV-1 and HSV-2) can be serious for infants, causing death or neurological impairment from disseminated infection of multiple organs and the central nervous system (47,68). Disease of the skin, eyes, or mouth can also occur (68). However, the highest risk of neonatal injury occurs when the pregnant woman acquires either virus type near the time of labor (69). The emotional and financial costs of vertical HSV transmission are obviously significant (31). The duration of the relationship is important, with an 8-fold risk in transmitting HSV-2 in relationships of one year or less compared to relationships existing for more than one year (8). Besides suppressive valacyclovir therapy, counseling, condom use, and abstinence are strategies that should reduce the risk of transmission. However, few discordant couples adopt safer sex practices when educated (70). Similar disseminated infections can occur in immunosuppressed individuals. Thus, such individuals entering relationships with HSV positive partners may benefit from suppressive therapy for the

source partner.

Finally, it is important to consider the degree of emotional stress in the source partner regarding transmission and the emotional problems that would likely occur in the non-infected partner upon acquiring genital herpes (71). Some individuals may have a more negative stigma regarding genital herpes than others and acquiring it would be severely damaging to these patients. Such patients should be counseled in an effort to help them understand genital herpes. Nevertheless, some couples' relationships may be severely affected by this disease and thus may require suppressive valacyclovir therapy more than other couples.

CONCLUSION

The high prevalence of genital infections with HSV-1 and HSV-2 is of great concern and indicates that a solution is required. Nevertheless, suppressive valacyclovir therapy is not a feasible method of reducing the incidence of genital herpes because of the overwhelming economic cost and issues of identifying asymptomatic individuals. Furthermore, the stigma and fear associated with genital herpes only increases the need to educate patients. If a symptomatic individual desires to take suppressive therapy, the physician must inform the patient about the influence of valacyclovir on transmission along with the probability that their partner will become symptomatic. Moreover, patients should consider certain factors that increase the importance of transmission when making a decision, such as the serostatus of the non-infected individual, type of HSV infection, duration of infection, HIV risk, HIV serostatus, pregnancy, and likely degree of resultant emotional stress. Finally, patients need to know about the realistic clinical harms of HSV infections. After better understanding the disease by discussing the above points, patients will be better positioned to make an informed decision regarding the use of prophylactic therapies like valacyclovir.

ACKNOWELDGEMENTS

I would like to thank Dr. Kevin Forward for introducing me to this topic and providing me with helpful suggestions and encouragement. Additionally, Dr. Dan Bunbury of the Cape Breton Health Research Centre provided a valuable review of my cost-benefit analyses.

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CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

Aftershock medicine: A Canadian returns to China following the 2008 Sichuan earthquake

Charles Jiang*

It had been an extremely busy morning at Jiuzhou Stadium, the impromptu hospital set up in order to tend to some forty thousand injured by the earthquake. I stood outside of our tent clinic, exhausted and drained. A young girl approached me, timid at first, but upon seeing my camera and realizing that I was a physician, she smiled. "Can I take a photo with you, doctor?" I recognized her as the granddaughter of a husband and wife I treated at the tent clinic the day before. "Sure, come here." I held her with one hand and my camera in the other. She was one of the thousands of survivors I encountered in the aftermath of the earthquake.

It is photographs such as this one that now stand to remind me of the excruciatingly long hours and unyielding effort that volunteers like my colleagues put into combating the wake of the disaster. On May 12, 2008, an 8.0-magnitude earthquake ripped through the Chinese province of Sichuan, leaving 69, 227 dead and many thousands more injured. When the news had finally reached me in Ontario, I immediately felt compelled to act. I contacted several other physicians in Ontario and began setting up a medical volunteer service team. Dr. Stanley Zhang, our representative from the Chinese Immigrant Emergency Relief Fund (CIERF), managed to allocate funding. After coordinating with the Canadian Medical Assistance Team (CMAT) from Vancouver, our team was beginning to take form; it consisted of an ER physician (Dr. Dave Ratcliffe), two family medicine residents (Dr. Haibo Xu and myself) and two paramedics (Dave Deines, Chris Kaley).

With no time to waste, we departed Toronto on May 17th and were on the ground in Chengdu, Sichuan early on the morning of May 19th. Our first priority was to contact the local health department in hopes of receiving official approval for our services. After a quick meeting with the local health department, we quickly realized that the local department was so overrun that it would have taken several days for us to get official approval. It became obvious we needed to look elsewhere if we were going to get involved any time soon.

It was decided that we should contact the Red Cross. The Red Cross enthusiastically accepted our help and sent us to Chaping, a severely damaged village, two hundred kilometers from Chnengdu. Our first day there was spent assessing local rescue capacity. We found out that there was a very well-organized rescue mission already in progress in the hands of the Chinese government, military and other Red Cross emissaries. The Chinese government's commendably expedient deployment of military rescue teams was undoubtedly a saving grace for many survivors, and tended to buy critical time for our team to treat injuries. Another prudent decision made by the government was to transfer the severely injured to hospitals in the nearby large cities of Shanghai and Shengzheng in order to reserve local hospitals' capacities in case another earthquake should follow.

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Based on our assessment of Chaping, CMAT decided to donate all of our medications to the local Red Cross and to change the focus of their mission. Dr. Ratcliffe and the two paramedics left Chengdu for Burma, equally as devastated by the earthquake but not as noticed by government emergency response authorities. Dr. Xu and I. however, decided to stay in Sichuan in order to continue our mission. We joined the independent organization "Global Doctors" in Mianyang, a Sichuan city devastated by the earthquake. We arrived in the middle of the night, and were greeted by a torrential rainstorm. The only hotel we managed to find had been so damaged by the earthquake that staying in it overnight, especially with the frequency of aftershocks, would certainly have been a death wish. Our only option was to sleep in a tent as did so many of the other survivors in the city. The rain drenched on our tent, and I could hardly sleep knowing we were finally so close to the people who were in need.

The next morning, we started work in Jiuzhou Stadium with doctors and nurses from around the globe. The stadium was able to accommodate 40, 000 injured survivors from Bei Chuan county. Unfortunately, we were still extremely undersupplied and were forced to create a medical tent with the spare medical supplies we had. Each physician provided medical care in five hour shifts; we encountered a vast range of medical and psychological cases. I was forced to draw on my years of training as a General Surgeon in China and a Family Medicine physician in Canada to treat everything from fractured bones to gastrointestinal complications to respiratory infections.

Our team worked around the clock in the stadium. We slept in tents. We ate the same food that was donated to the earthquake victims. We would periodically experience the horror of aftershocks, and witness the joy of saving a patient's life and the sorrow of losing one. After several days, our team gained a new respect for the resilience of the earthquake survivors who were so brave after losing everything from their jobs, their homes to their families. It was an incredible honor to be of service to them.

I believe that this catastrophe was a learning experience for all parties involved. The citizens of Sichuan learned that even in the face of devastating evil, there is hope. The Chinese government learned how to organize and deploy massive rescue efforts. They also learned the benefits of allowing foreign aid – they did not repeat the mistake they made following the 1976 devastating earthquake in Tang Shan when they refused to such aid. This was also the first relief mission Dr. Xu and I participated in, and the experience gained from our work in Sichuan is truly immeasurable.

ACKNOWLEDGEMENTS:

It would have been impossible to complete such a relief mission without the support and service from individuals and organizations in China and across Canada. I would therefore like to acknowledge the work of CIER (Toronto), CMAT (Vancouver), Global Doctor (China), CCNC (Chinese Canadian National Council), DRAG (Disaster Relief Action Group) and UNICEF (United Nations Children's Fund, Montreal). The individuals to whom I am eternally grateful include but are by no means limited to Dr. Stan Zheng (Toronto), Mr. Victor Wong (CCNC), Ms. Alice Choy (CCNC), Dr. Joseph Wong (Toronto), Jack Layton M.P., Mr. Alan Hamson (Vice-Consul, Embassy of China), Dr. Ming Mao (Sichuan Huaxi 2cd hospital, China), and Mr. Julian Z. Xue (McGill University). We appreciate the generous assistance from Mr. Frank Shi, Mr. Liuyu Zheng and Mr. Ruo's family in Sichuan. Special thanks to Ms. Fei Yu who donated the rental of a satellite phone for us. Many thanks also to Todd Plummer and Andrei Liveanu from the McGill Journal of Medicine for extensive reviewing and editing of my manuscript. Finally, a salute to all WEPAT members. I would like to dedicate this report to my family, whose unending support gave me the courage to complete this mission.

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CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

Evidence Based Medicine in Cultural and Historical Context

(Julian) Zhunping Xue*

It is difficult to argue with the fundamental tenet of Evidence Based Medicine (EBM), the c*onscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients*[i]. What sane, ethical person or culture can deny something so obvious? As members of a dominating society, however, we forget how current practices derived from the past and we mistake the present to be the only possibility[ii]. Looked across time, EBM is the perfectly unique product of the West, embedded as we are in rationality[iii], and our particular brand of EBM, steeped in rational methodology: RCT, meta-analyses, guidelines and quantification[iv], is far less universal than we might believe.

Cries for EBM can be found as early as the late 18th century, but its modern carnation began in the 70's with figures such as Dr. Arthur Cochrane and John Wennberg[v]. They denounced medicine as practiced then, based upon expert consensus and mental models which did not bear upon reality[vi]. Existing evidence must be organized and used, they reasoned, and the need for new and better evidence also became apparent. This is progress in all senses: they managed to reduce an immense cognitive dissonance within our society, a dissonance that leads laypeople to scratch their heads and ask: "…and what were they doing before that?"

Since then, EBM has spread with immense speed, but also have had its fair share of critics[vii]. Many explanations are given for this conflict, from a "sociology of professions"[viii] to lingering suspicions of laziness and closed-mindedness (by both sides), but one itch was never scratched: perhaps EBM is not culturally neutral. Perhaps it is a product of our Age of Reason[ix], one of its crowning jewels, and its strengths and weaknesses are reflective of our society as a whole.

Our culture uniquely worships efficiency and certainty under the umbrella of rationality. In the classic narrative, we have come to this through a triumph of science as well as struggles for a more reasonable society against a whimful aristocracy[x]. That almost all the evidence in EBM is used to further these goals cannot be called a coincidence; this is the deliberate (if often blind) action of a willful society. Evidence does not form its own goals! Indeed, evidence funded ill aims

i - This definition is quite prevalent, see the beginning of Eddy 2005 (1) for example.

ii - Daniel Dennett (a famous living philosopher who thinks deeply about religion, evolution, and consciousness) likes to say do not mistake a failure of imagination for impossibility. See (2) for an example.

iii - This hardly warrants a reference, but John Ralston Saul has attacked rationalism so spectacularly that I feel compelled to direct readers to his book Voltaire's Bastards (3), chapter 4, where Saul traces the beginning of rationality to the Inquisition

iv - To be convinced, one merely needs to leaf through (4), which is almost completely methodological and devoted to RCT's and the like. However broad EBM is defined in philosophy, these methods are how it plays out in practice in our particular society.

v - This brief history of EBM is compiled from (1) and (5)

vi - Goodman (5) is especially vehement about previous medical practice. On page 6: *This percentage [of evidence-based practices] is always very low – it ranges from 10% to 25% of medical decisions. The numbers leave us slack-jawed. If clinicians decisions are based on (high-quality) evidence only 10% or 25% or even 50% of the time, then what on earth is guiding the rest of the decisions in which pain, suffering, disability and life hang in the balance?*
Even Eddy (1) caricaturizes earlier practice with the physician as a trusted all-powerful being who in fact had little idea what they were doing. Although I cannot evaluate those years directly, such mocking makes me suspicious of historical rewriting of science by the victors, a la Kuhn (6). I have yet to meet an entire society of idiots.

vii - See (7). It raises suspicion that something so "basic and obvious" (5, p.7) should meet so much trouble. It's much too easy to slap the trouble with "ignorance".

viii - This is the explanation given by (7). I find it somewhat naive.

ix - I found this phrase from Saul (3). My own world view is strongly influenced by Saul and Kuhn, as might become obvious throughout this essay. Although I do not agree with Saul in his extremism, I feel he really reaches the root when discussing the "dictatorship of reason" as the heart of many ills of modern society.

x - Saul (3), chapters 1-5.

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in the past: Hitler's eugenics program was proudly based on statistics and eugenics itself was initiated by Sir Francis Galton, who cannot be accused of Hitler's political agenda[xi]. Yet who speaks of eugenics today?

Although all proponents of EBM speak of patient wellness, that wellness is phrased in terms of efficiency (low cost – high delivery), reducing uncertainty in physician decision making, and a rationalization (that is, a logicization) of the medical process from research to bedside[xii]. These goals themselves, however, are dictated by our beliefs and culture – by rationalism. Even if there is data that patient outcomes are improved by EBM[xiii], one cannot ignore the constant grumbling by the general public of the inhumanity of scientific medicine – in the words of Paul Nadler, director of the film *Braindamadj'd*: "when doctors see me, they see the 5%, that I have 5% chance of recovering, they see what they expect. They don't see the human, the me, the whole person."[xiv] This means that other goals are possible and laudable. They in fact belong to another cultural strand that existed within Western history alongside rationalism for many years: humanism.

When doctors advocate for whole-person care, when doctors lament the time pressures they work under, when patients complain bitterly about medical arrogance, they do not battle EBM, rather they battle the cultural network, rationalism, within which EBM is embedded. That is why combatants of both sides seem to talk over each others' heads: as protestors push against EBM, EBM supporters are bewildered: there is nothing in their cultural framework that could possibly negate EBM; protestors who are meshed in humanism, however, strive for very different goals, and they are bewildered because a tool is suddenly deciding goals – grossly inappropriate actions for a tool.

Carefully dissected, the deepest criticism of EBM all lie here: not EBM as a tool, but of the rationalistic weaknesses underlying EBM. Examples include how many questions are unanswerable in EBM, how important patient experiences are not included in EBM, how EBM is often misinterpreted and misused[xv]. The flailing against EBM is therefore a flailing against the culture of rationalization, a strong, ubiquitous current in our society. In this view, EBM is a powerful tool that predisposes us further towards that potentially dangerous current.

Is this rationalizing current dangerous? Yes it is[xvi]. We sense far more than we can measure. Indeed, we sense far more than we can paint, sing, write. We all sense more than any culture can synthesize; each culture emphasizes a coherent portion of our sensed world. In the West, we have chosen measurement. For all its triumph, this done in excess will dull our other senses and we are reduced to sensing only that which we can measure. Extreme rationality impoverishes our abilities to empathize, to doubt and be heterogeneously human, and that trend we do not only see in medicine, but witness in the West as a whole. The reduction in doubt is particularly dangerous, as no self-correction can occur – a typical EBM answer to any problem is: more, better EBM. Yet that extra evidence requires resources to gather[xvii], an opportunity cost that is difficult to measure and therefore never evaluated (we sense what we can measure). Moreover, a focus on efficiency leads towards homogenization – indeed, variation in medical practice is used to justify EBM, which proposes ironing them out [xviii]– and an adversarial relationship between doctor and patient, exacerbating our willful blindness.

xi - I found (8) to be a generally excellent discussion of eugenics. I shamefully also used Wikipedia for this discussion. I owe it to Chenjie Xia (med 4) for bringing this point to my attention.

xii - Elements of these things can be found in any writing supporting EBM, (7) and (9) provide ample reference.

xiii - The evidence is usually weak. Goodman nicely backs off on this point, he really does care about evidence. On the back of his book is printed: "At its core, evidence-based practice rests on a supposition which, while probably true, itself has unclear evidentiary support". For me, what is more important is that even if EBM does provide a significant improvement to patient well-being, if that improvement is not immense, the we will always be left with the nagging question: what if we had directed all the resources currently in EBM into another endeavor – say, teaching doctors rhetoric? This sort of opportunity cost is immeasurable. Bad practice as it is to wonder about "what-if's", I just want to illustrate that this kind of decision (i.e. to go with EBM) cannot itself rest on evidence; we progress by scratching cognitive itches as they rise.

xiv - Talk and discussion with Paul Nadler, at the showing of his film Braindamadj'd, the second film of the Films that Transform series by the Whole Person Care center of McGill Medicine.

xv - These are directly quoted from (4), section "Limitations of EBM", p. 149. Curious to note here is that the solution to many limitations as given is "new and better EBM".

xvi - I again follow Saul here. If one reads the body of Saul's work, it's difficult not to be convinced of this point.

xvii - McGovern (4) notes this as a limitation of EBM: EBM favors interventions that attract commercial sponsorship. EBM is good for… …those [disorders] that require a treatment or intervention that has a commercial application. Performing major RCTs properly is expensive and non-commercial research funds are scarce… …Many potentially effective, and possibly cheaper interventions will not receive health service funding because the 'evidence is not good enough', since there was never enough money available to test the intervention properly.

xviii - Saul (3) notes that …our economic system does try to produce the maximum quantity of goods… blunt edged products which can be aimed down the center line of established taste, flood the marketplace with… identical goods… battle of the market place cannot turn, then, on the public's comparison of products. Instead, it revolves around invisible organization strategies and visible packaging and publicity. Although medical practice is very different from a regular commercial good, the above somehow alarmed me in relation to modern pharmaceutical companies. How much a drug succeeds depends at least as much upon the maneuvering by its producing company as by its own merit. However, this is the logical conclusion of a rational

Of course, the above does not have to happen, one can, in principle, have both rationality coupled with humanity. On the other hand, rationality, especially in our society, certainly predisposes us to such impoverishment. Some of this trade-off is simple: as molecular receptors, RCT's and genomes float to the collective medical consciousness, other things sink to the bottom. We medical students no longer read Osler as our peers did decades ago[xix], we can no longer quote the classics as Osler did with such ease, and he did so with every expectation that his listeners – often students like us – will be familiar with them. Other parts of trade-off are more subtle: the increase in certainty, the illusion that EBM is medicine or is what medicine strove to be across all time, means that the physician is less likely to struggle with the cosmic questions. Without this struggle, this is no motive to look to history, philosophy, and thereby mark one's own place in time. This loss of literature and historical perspective, primary vehicles of humanism, means that we are even less likely to be introspective, to assess and reflect upon the world, and yet these traits are vital to humanistic medicine.

The controversy of EBM is thus a cultural tension being felt on medical turf. EBM itself is a cultural-specific product, a child of rationalism, its goals are determined by rationalism and its methodology reflect both rationalistic strengths and weaknesses. Doubtlessly it is EBM-like practices that gave us hygiene[xx] and the germ theory of disease, doubtlessly EBM is at least partially responsible for medicine's loss of humanism.

A fun test for the role of culture and history in medicine is that of the Martian anthropologist on Earth. Sadly, I cannot go so far and the furthest vantage point I can manage is that of a Chinese Taoist. Zhuangzi[xxi], that dreamer of butterflies and great expositor of Taoism after Laozi[xxii], once said: *life is finite, but knowledge is infinite. To pursue the infinite with the finite, how dangerous that is! To believe that one truly knows, how extremely more dangerous that is!*[xxiii] Taoists downplay the importance of knowledge and would be horrified at EBM, yet they are sane and have a deep, satisfying and coherent philosophy. They dislike knowledge because it distracts from the Tao, the universal Path that we can experience if we but stopped and experienced it. Mystic, yes, but wise also, I think, because formed knowledge dulls that which we cannot include in knowledge per se but can sense – be it empathy or Tao. The opening of those senses is, I believe, the path to enlightenment, which, in my opinion, is almost culturally-neutral.

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society with rational production. Homogeneity ensures efficiency.

In fact, that our medical care is often variable is often used as a justification that we need EBM (1, 5, 9). This taken to extreme is again dangerous; it is a fallacy that reason and logic can necessarily only lead to a single decision. Such uniformity is a part of the rationalist's dream, but unlikely to be a part of the world proper – even with perfect knowledge.

xix - In fact, the Osler lecture was embarrassing in exposing how little we knew about this great man and his works, despite being at the touted home of Osler. I read the Aequinimitas soon after, and I was deeply moved by many of Osler's passages – particularly how we are "simply stage accessories in the drama [of our patients' lives]... picking up, here and there, a strutter, who may have tripped upon the stage." It is a humbling thought. I know McGill students, at least of the Osler club, read and thought Osler long ago. No parallel exist today.

xx - Goodman (5), p. 79: "...it began, of course... with Florence Nightingale and her systematic data collection ... improved sanitation would save the lives of hospitalized soldiers during the Crimean War. Her reforms ... met opposition – can you imagine it? – and it took epistemological cudgel on the order of "Those who fell before Sebastopol by disease were above seven times the number who fell by the enemy..."

xxi - I read the Chinese version, but a fair English translation can be found in http://www.religiousworlds.com/taoism/cz-text1.html, based on a translation by Herbert A. Giles. Zhuangzi is commonly thought to be the second great father of Taoism, and one of the greatest story tellers of ancient China, being extremely pithy and witty, while profound at the same time.

xxii - Zhuangzi's most famous story is one where he dreams he became a butterfly, and when he woke he is unsure whether he was dreaming the butterfly, or now the butterfly is dreaming of being Zhuangzi. Laozi is the founder of Taoism, and wrote the Dao De Jin, the primary text of Taoism.

xxiii - This is my own translation. The online translation is: Human life is limited, but knowledge is limitless. To drive the limited in pursuit of the limitless is fatal; and to presume that one really knows is fatal indeed! My translation differs primarily on the character殆, which online was translated as fatal. But death holds no fear for the Taoist, it is merely a part of the Tao. I translated the word as danger, which holds true to the etymology of the word, which derives from怠, or carelessness.

xxiv - Tao literally means "path" in Chinese

CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

Medical Leadership: Doctors at the Helm of Change

Nicholas Chadi*

INTRODUCTION

Since the beginnings of the modern era, medicine has evolved tremendously. Merely two hundred years ago, American and European medical treatments were generally provided by independent physicians who went from home to home to offer their services. From this form of medicine, often referred to as "bedside medicine", (1) Western countries started to move towards a more centralized form of medical care provision: hospital medicine. During the 20th century, as cities steadily grew larger and more populated, numerous hospital supercomplexes with complicated hierarchal structures emerged. Employing hundreds and sometimes thousands of health care professionals, hospitals became increasingly difficult to manage and required the presence of a well organized management staff.

With the current aging of Western populations, developed countries now face major problems within their healthcare systems concerning economics and efficiency. Having to deal with the consequences of a strong movement of medicalization over the past few decades that has brought more and more elements of everyday life under medical jurisdiction, (2) Western governments are now struggling to restrain the rising costs of their national healthcare coverage. Seeking new venues and solutions, many countries like Canada allocate an increased importance to practices such as preventive medicine, surveillance medicine and homecare treatments. (1) All three of these practices tend to reduce the role played by hospitals in healthcare. However, hospital treatment remains an essential part of Western healthcare programs, and the development of parallel structures does not eliminate the management issues that health ministries are faced with.

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Within hospitals and clinics, many aspects of the physician's daily routine have changed dramatically during the past generation, adding another level of complexity to the management of healthcare. Both in Canada and abroad, doctors are increasingly unhappy with the way they are managed. A main cause of physician dissatisfaction lies in the fact that "the individual orientation that doctors were trained for does not fit with the demands of current healthcare systems." (3) Faced with numerous problems like "funding constraints [and] demand[s] for greater accountability for the safety, the quality and the efficacy of healthcare," (4) doctors are more and more frustrated with their daily workload and don't feel as appreciated and supported as they might have been in the past. Physicians frequently receive instructions regarding these new demands from leaders who either do not possess a clinical background or do not wish to occupy the leadership role they are occupying. Hence, the lack of clear and reassuring guidance coming from respected and qualified professionals affects doctors as much as the overall well-being of the whole Canadian medical system.

Striving to improve the efficiency of their healthcare systems, health ministries of countries such as Australia, the United Kingdom and Canada often hold hospital management teams accountable for the increases in healthcare spending. (5) In blaming hospitals, these countries uncover an ongoing problem that is causing more and more trouble to health ministers worldwide. In fact, Bruce Dowton, the Dean of Medicine at the University of New South Wales explains that "[d]espite leadership roles being critical, [Western governments] persist with outmoded models of organizations and pay inadequate attention to developing individual leaders and new models of leadership within the medical profession". (4) In other words, as Dowton suggests, hospital inefficiency could realistically be eliminated by training healthcare professionals adequately in the area of medical leadership. Thus, in order to face current and future changes in healthcare, Canada needs to develop a new

generation of competent medical leaders involved at all levels of its healthcare system. Many countries worldwide are starting to acknowledge the numerous advantages of developing leadership skills in their medical students, physicians, CEOs/CMOs and health ministers. In Canada, although some promising initiatives have already been taken, much still needs to be done in order for the healthcare system to benefit from strong medical leadership.

MEDICAL LEADERSHIP

"Medical leadership" has only recently started to take its place as a common medical term. As Dowton noticed four years ago, "leadership has received little attention in […] peer-reviewed medical literature." (4) By definition, medical leadership consists of having fully trained physicians occupying leadership roles relevant to the practice of medicine. Physician leadership can include resource managing, decision making, recruiting and medical consulting as well as implementing changes and improvements in hospital and clinical settings (6). Medical leadership also goes alongside with adequate team building activities and an appropriate sharing of decision power. (7) In this perspective, there is no room for an all powerful CEO (Chief Executive Officer) having nothing in common with the team he is leading. On the contrary, good medical leadership intrinsically depends on the acknowledgement of the important role of all the levels of healthcare workers involved in the functioning of a hospital. (7)

Countries around the world are starting to realize the importance of good medical leadership. Although Canada is slowly starting to recognize the importance of training good medical leaders, other countries like the Netherlands, Denmark and especially the United Kingdom are a step ahead in initiating a wave of changes inside their respective healthcare systems (8). In Great Britain, the National Healthcare Services (NHS) is well aware of the importance of training competent medical leaders. For example, in a recent public report, J. Clark and C.M. Morgan, two physicians working at the NHS headquarters, wrote that the improvement of the British healthcare system through the successful implementation of current and future medical reforms "is very dependent on the support and active engagement of all doctors, not only in their practitioner activities but also in their managerial and leadership roles". (9) Thus, British healthcare ministers understand that fully trained doctors must be involved in all the levels of the country's medical structure in order for optimal changes to take place.

Although coping with a very different healthcare system, American medical associations, governments and private healthcare consortiums also recognize the urgent need to involve physicians in all future medical reforms. Richard W. Schwartz, a physician working for the Kentucky College of Medicine who possesses an MBA, states that "precisely because they are at the center of clinical service and delivery, physicians are the ideal leaders for healthcare in the 21st century". (10) Hence, being the ones who are the most aware of the changes needed in national medical systems, physicians must not be swept aside in the implementation of measures that will directly affect their daily work.

Furthermore, the NHS has already taken concrete measures to implement good medical leadership in all levels of its medical structure. In fact, the same report cited above explains that in the UK, "there are some exciting medical management and leadership initiatives being introduced both locally and nationally in both undergraduate and postgraduate training" (9). Through its integrated approach to medical leadership, the UK brings forth the importance of developing good physician leadership at multiple levels.

Considering the similar challenges faced by both the British and Canadian healthcare systems, four different levels of Canadian healthcare medical professionals could strongly benefit from improved medical leadership: students, physicians, health executives and health ministers. In their respective scopes of activity, all four of these healthcare actors play an equally important role in solidifying Canada's medical hierarchy.

MEDICAL STUDENTS: LEARNING TO BECOME MEDICAL LEADERS

Currently, very little importance is given to medical leadership in Canadian medical curricula. Medical admission procedures, including individual interviews and autobiographical letters, focus mostly on uncovering qualities like empathy, determination and intelligence as well as skills that are used by physicians when practicing their traditional medical role. However, universities most certainly represent the best location to target, develop and train competent medical leaders for the future. In order to reach this goal, common leadership skills must be looked for in medical school applicants. In an article entitled "Physician Leadership," Dr. Woo explains that qualities like "vision, ability to sacrifice and courage" (11) represent skills that are mandatory for any leader and should not be forgotten when recruiting future doctors. While most common leadership skills might at first seem like essential assets for any good physician, some of them could be seen as conflicting with the qualities that are actually targeted by Canadian universities. For

example, while a well-performing corporate leader must aim for profit and time efficiency, practising physicians must show empathy and care for their patients. For students wishing to become both good physicians and efficient leaders, the time-saving vs. quality of care duality represents a major dilemma. In the financially constrained reality of the Canadian healthcare system, this is a problem that every physician must cope with when undertaking new leadership roles. However, through the training they receive in medical school, doctors are taught to understand human nature like no other professionals. Considering this advantage, medical students should certainly be able to become both competent leaders and well estimated physicians if they are given the opportunity to develop the appropriate skills. Hence, if medical school applicants are to occupy leadership positions during their career, they must be chosen according to their leadership capacities. As for adequate leadership training, it must be integrated into medical curricula.

PHYSICIANS: INTEGRATING GOOD MEDICAL LEADERSHIP IN EVERYDAY PRACTICE

Physicians' professional activities require them to be good team leaders. In fact, doctors working in both clinics and hospitals lead small groups of healthcare professionals on a daily basis. While the teams they are responsible for might seem small, physicians nonetheless need to demonstrate essential leadership skills. When they work in a large hospital setting, they also have to be able to execute directions issued by their superiors appropriately to assure the fluidity of inter-staff relationships and the well-being of the hospital's work environment. Thus, most doctors are constantly involved in situations where they need to both be able to manage and be managed. However, while physicians can be perceived as "smart individuals whose long-term vision sustained them through years of gruelling education" (12) this does not necessarily make them the best team leaders. To help them become the leaders they are well capable of becoming, Canadian health institutions must then strive to offer adequate continuous medical leadership training to their practicing doctors. In their leadership tasks, physicians must rely on three main qualities which form the basis of medical leadership: the capacity to work in teams, the ability to personify essential leadership skills and possession of a strong emotional capacity.

First, since the ability to work well in a team is not necessarily something that is readily teachable in schools, hospitals must seek to provide adequate training workshops to their physicians and implement measures that will allow them to feel more comfortable inside the existing leadership structure. For instance, healthcare institutions can seek to create physician advisory committees that include both management staff and physicians. This way, doctors can get more involved in the functioning of their hospital (7) Also, this would make it easier for them to create positive group dynamics in their own everyday leadership spheres.

Second, the NHS Medical Leadership Competency Framework suggests that all doctors should be able to excel in five different domains: "Personal qualities and professionalism, working with others, managing business, transforming services and setting directions." (13) While the first two skills are often mastered in medical school, the last three, being directly related to management and requiring practical experience, must be introduced to practicing physicians all through their career. Since very few doctors have the opportunity to complete an MBA, continuous education and training must take an important part in developing adequate medical leadership for active doctors.

Third, in order to become sensitive leaders, doctors must learn to master their emotional intelligence, also called "EQ". Including aspects like "self-awareness, self-management [and] social awareness" (12), emotional intelligence allows doctors to act as realistic and efficient leaders that can bring a larger contribution to their work team.

HEALTH EXECUTIVES: CEO VS. CMO

In order for hospitals to function efficiently, they need to be led by a strong and capable management team. In developed countries, very few Chief Executive Officers are from a clinical background and even fewer of them are medically qualified. While it would definitely be optimal for all hospitals to hire their directors among candidates issued from the medical field, it seems impossible in the short term. In the meantime, including empowered Chief Medical Officers (CMOs)—practicing physicians—in all hospital management teams might prove to be a good alternative. Overall, the CMO can be seen as a facilitator who allows a better interaction between the hospital healthcare professionals and the management team. In other words, "The CMO generally has specific duties related to the management, direction and evaluation of quality initiatives and clinical affairs, but is increasingly involved with the strategic planning and relationships with critical physician groups." (8) In Canada, there are very few CMO positions available. Considering how much positive input they could bring to any large hospital, it is essential that Canadian ministries look into creating more CMO job opportunities.

MINISTERS OF HEALTH: A NEED FOR INSPIRATIONAL LEADERS

For captains of well-run ships, it is essential to understand the tasks accomplished by all of their crew members. It is equally important for the heads of the Canadian ministries of health—both national and provincial—to be in tune with the professionals working under them. The present minister of health in the province of Quebec, Yves Bolduc, and his predecessor, Philippe Couillard, are both experienced physicians. However, having experienced physicians working as national or provincial Ministers of Health has not been the dominant pattern during recent decades. The same problem also prevails in many other developed countries; the Austrian Minister of Health Andrea Kdolsky was once a famous physician and is now at the head of one of the world's top performing healthcare systems, but the British, American and German Ministers of Health do not have any relevant clinical expertise. It is in the best interests of all parties involved that a healthcare professional himself or herself be at the helm of any healthcare system.

CANADIAN HEALTHCARE: PROBLEMS AND SOLUTIONS

In Canada, although fundamental problems regarding the implementation of strong medical leadership are still very present, many promising initiatives are starting to emerge. First, in its official publication of the 2005 CanMEDS standards, the Royal College of Physicians and Surgeons of Canada established a thorough description of the seven essential skills that should guide the practice of all Canadian physicians. Among the seven standards listed (all of equal importance), "manager" appears in the fourth position and is defined as such: "The CanMEDS Manager Role describes the active engagement of all physicians as integral participants in decision-making in the operation of the healthcare system." (14) While this might seem like a proof that Canada is now embracing a new movement towards better medical leadership, it has to be noted that CanMEDS standards only serve as guidelines for medical curricula and do not have any true legislative or reformative power.

Second, the Canadian Medical Association has recently started to offer intensive leadership programs and workshops through its Physician Manager Institute. Open to all physicians and medical students, the core leadership program which comprises five 3-day intensive sessions is described as the following: "Through these highly interactive workshops, [physicians] will learn how to lead and manage change, transfer best practices into action, inspire excellence and sustain productive relationships at all levels in [a] hospital or health organization" (15). Even though these workshops are easily accessible and offered all across Canada, they are fairly costly (close to 1500$ per workshop) and aren't equally recognized in Canadian hospitals. Furthermore, very few incentives are provided to doctors or future doctors who consider pursuing this leadership training.

Third, medical programs in universities all around Canada are starting to offer the option of taking management classes as elective credits during the four years of formal medical education. Among Canadian universities, McGill is a pioneer in this domain. In 1996, McGill developed a joint MD-MBA program that is still unique in Canada. Aiming to train fully recognized physicians that will also acquire strong management training through the completion of a health-oriented MBA, this program is defined by the McGill Faculty of Medicine as "a five-year program that prepares graduating physicians for leadership positions in the health care sector." (16) Although it was originally meant to accept at least five students every year, only 2 students were admitted to the MD-MBA program in 2007 due to a very small number of applicants. This is a proof that much still needs to be done in order to attract more competent medical leaders.

Even though legitimate initiatives aiming to develop a new generation of medical leaders seem to be well initiated, many fundamental problems still affect the Canadian transition towards more comprehensive medical leadership. For example, in most hospitals, there is a huge and complex bureaucracy that revolves around hospital directors who are often disconnected with physicians' needs and requirements. As stated by Dowton, "in many settings, implementation of sound policy appears to be in danger of falling into a morass of hierarchically driven bureaucratese, involving a blame-prone audit driven by paper-based compliance." (4) While doctors should be the ones involved in implementing healthcare reforms, resolutions and concrete plans are left in the hands of bureaucrats who often fail in adequately communicating with the ones who will be leading the actual changes. This underlines an omnipresent duality that prevails between doctors and CEOs: physicians do not want to get involved with CEOs who don't truly understand their reality. Also, in the few cases where potent leadership positions are held by qualified physicians, management tasks are often seen as a punishment. For instance, in Canada, leadership positions are far from being valued by the medical society and the unfortunate physicians forced to assume them are often compelled to accept dramatic drops in their salary.

In addition, being a full-time medical manager is not usually considered a possible career path by medical

school graduates. Since very few job opportunities allow fully trained doctors to both make use of their medical skills and act as respected medical leaders, it is very difficult for a doctor to commit to a full-time management career. (8) Furthermore, the few Canadian physician-leaders frequently can not take part in realizing the global vision of the hospital they are working for as they are working under health ministers or executives who most often are not associated with the medical profession. It is hence not very likely that doctors who have just completed up to 10 years of demanding medical training will accept to struggle in a work setting where their newly acquired competences aren't truly valued.

CONCLUSION

In conclusion, the Canadian medical system faces many new challenges that require ambitious health reforms. As many countries begin to realize the importance of good medical leadership, Canada must put an increased effort into developing a new generation of competent and efficient medical leaders. In doing such, Canadian health ministries must acknowledge the importance of training accomplished medical leaders at all levels of their healthcare structures: the student, the physician, the executive and the government official. Having already shown a certain number of promising initiatives related to the implementation of medical leadership, Canada must renew its efforts to overcome many fundamental problems that are still very present in the national healthcare system.

In order to give Canadian healthcare a more comprehensive and solidly led structure, many immediate measures can be envisioned. Among the different ways of improving national medical leadership, five suggestions particularly apply to the Canadian context: (i) offering an increased recognition to doctors undertaking leadership positions, (ii) offering higher wages and greater incentives to motivate future doctors to orient themselves towards health-related management careers (iii) selecting more medical students who have the ability to become great leaders (iv) integrating medical leadership training in all steps of medical education, and finally, (v) privileging the filling of medical leadership positions by managers who have a solid clinical background. Currently, Canada has one of the most comprehensive and inclusive healthcare systems in the world. Canada is also considered as one of the countries offering the best overall living conditions. (17) To keep its place as a global leader in terms of the quality of life it offers to its citizens, Canada must not hesitate to follow the path leading to solid and well sustainable medical leadership.

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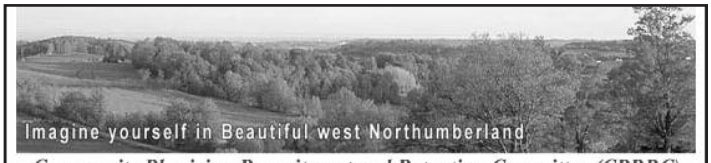

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FOCUS REVIEW

The effects of outdoor air pollution on chronic illnesses

Hong Chen and Mark S. Goldberg

Chronic diseases, especially cancer, cardiovascular disease, and respiratory diseases, are the leading causes of morbidity and mortality worldwide. In Canada alone, chronic diseases account for 87% of total disability and 89% of all deaths (1). It is estimated that half of the Canadian population live currently with a chronic illness and more than 90% of them have these three diseases (1). Chronic diseases develop typically over long periods of time and have multiple risk factors. The major causes of cardiovascular disease include high cholesterol, high blood pressure, and obesity (2-6). For lung cancer and respiratory disease, tobacco smoking and exposure to toxic chemicals are important risk factors (7-15). More recently, ambient air pollution has been implicated in increasing the incidence and mortality from lung cancer and from cardio-pulmonary diseases (16-19).

Present-day urban air pollution comprises hundreds of substances, including sulphur dioxide, ozone, nitrogen oxide, nitrogen dioxide, carbon monoxide, carbon dioxide, particulate matter, rubber dust, polycyclic aromatic hydrocarbons, and many different volatile organic compounds. Particles are a heterogeneous mixture of solid and liquid droplets with wide distributions of size and mass. Coarse particles, greater than 2.5 μm in median aerodynamic diameter, derive from a variety of sources including windblown dust and grinding operations; fine particles are primarily from the combustion of fossil fuels (20). Common constituents of particulates include elemental and organic carbon, sulphates, nitrates, pollen, microbial contaminants, and metals (20). Fine particles can react with sulphur dioxide and oxides of nitrogen in the atmosphere to form strong acids, such as sulphuric acid, nitric acid, hydrochloric acid, and acid aerosols (20). In addition, urban air also contains benzene and 1,3-butadiene that are considered carcinogenic (21).

The health impact of outdoor air pollution became apparent during the smog episodes in London, England, (Figure 1) in the 1950s and in some other places. In London, the lethal fog, which occurred because a temperature inversion trapped heavy combustion-related emissions of particles and SO2 (traffic and coal-fired heating), resulted in approximately 3,000 more deaths than normal during the first three weeks of the smog event (Figure 2) (22). During five days of a smog episode in Donora, Pennsylvania, a small town of 14,000 residents, 20 people died and over 7,000 were hospitalized (23). These episodes demonstrated conclusively that the confluence of adverse weather conditions and extremely high levels of pollution from ambient particles and sulphur dioxide can cause immediate and dramatic increases in mortality (24;25).

In the subsequent decades, especially in economically developed countries, changes in fuels (e.g., low sulphur fuels), improved combustion technology, and regulations (e.g., the clean air acts in the UK, USA, and Canada) have led to significant reductions in the levels of ambient air pollution (Figure 3). Unfortunately, the situation in some other less developed countries is not encouraging. For example, Delhi, India, is subjected frequently to high levels of total suspended particulates, with an annual mean concentration well exceeding 600 μg/m3 (26). In many other parts of the world, such as Mexico City and Beijing (Figure 3), similarly high levels of total suspended particles are observed frequently (27;28). In contrast, the maximum annual

Figure 1: The London smog episode of 1952. A photograph during the day.

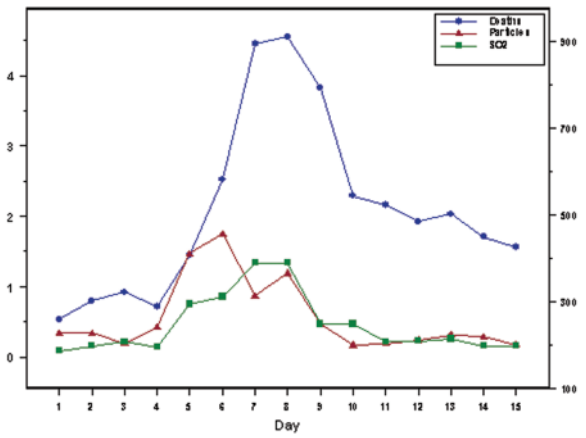

Figure 2: The association between total suspended particles, sulphur dioxide, and nonaccidental deaths during 15 days in the London smog episode of 1952. The right hand vertical axis shows the number of deaths per day and the left hand axis represents concentrations of the two pollutants, on a relative scale.

level of total suspended particles in Windsor, Ontario, one of the most polluted cities in Canada, is usually below 120 µg/m3 (29).

THE EVIDENCE

Over the past 25 years, considerable epidemiological research has been conducted to investigate acute and chronic effects on health as a result of exposure to ambient air pollution. The bulk of this work has been focused on health effects from short-term (i.e., day to day) fluctuations in ambient levels of pollution. Associations have been found between exposures occurring on the day of the event or the preceding days and daily non-accidental mortality, cardio-respiratory deaths, hospitalizations, and emergency room visits (30-50). There is also evidence that certain subgroups of the population are at higher risk. The conclusion is clear: short-term elevations of ambient air pollution cause a variety of acute health events, especially in certain subgroups of the population, such as the elderly, children, and those who are impaired physiologically (e.g., congestive heart failure, diabetes, and cardiovascular disease) (47;51). In contrast, the effects of air pollution on chronic diseases have not been studied as extensively. This is due to the difficulty of assembling large cohorts, following subjects through a long enough period of time, and the difficulty in measuring personal exposures to ambient air pollution.

We have recently completed a structured review of the association between long-term exposure to ambient air pollution and the risks in adults of nonaccidental mortality and the incidence and mortality from cancer and cardiovascular and respiratory diseases (52). A total of 17 cohort studies and 20 case-control studies, published between 1950 and 2007, of the long-term effects of air pollution were identified. We abstracted characteristics of their design and synthesized the quantitative findings in tabular and graphical form. We estimated "summary" relative risks for exposure to certain frequently measured specific pollutants by combining statistically the estimates from the different studies. We also assessed whether there were large variations in the estimates of relative risk between studies (referred to as "heterogeneity").

Our analysis of the published studies showed a 6% increase in non-accidental mortality for every increase of 10 µg/m3 of fine particles, independent of age, gender, and geographic region. This was derived from a log-linear exposure-response pattern; that is, mortality increased exponentially with increasing concentrations of fine particles.

This result can be translated to an estimate of an additional risk in nonaccidental mortality of 1.8% for residents of Windsor, Ontario (annual mean concentration of fine particles: 13 µg/m3) (53), a 16% increase in risk for residents of Mexico City (annual mean of fine particles: 35 µg/m3) (54;55), and a 96.6% increase in risk for residents of Delhi, India (annual mean of fine particles: 126 µg/m3) (26) as compared with those who were exposed to 10 µg/m3 of fine particles (World Health Organization recommended long-term guideline value for fine particles) (56).

We also found that long-term exposure to fine particles was associated log-linearly with an increased risk of mortality from lung cancer (range: 15%-21% per a 10 µg/m3 increase) and overall cardiovascular mortality (range: 12%-14% per a 10 µg/m3 increase) (Figure 4). In addition, we found living close to highways or major urban roads appears to be associated with elevated risks of these three health outcomes. For the other pollutants and health outcomes, data were not sufficient to draw any meaningful conclusions. (57-62)

At first glance, the magnitudes of these associations are smaller than those of some other risk factors, such as smoking. For example, smoking 1 to 14 cigarettes each day was associated with a six-fold increase in risk of dying from lung cancer (63) and a two-fold increase in fatal coronary heart disease (64;65). It is impossible to compare these relative risks directly as the metrics of exposure are different. Because population exposures to air pollution are virtually ubiquitous, there is a very large impact on chronic illness due to exposure to ambient pollution.

NUMBER OF PERSONS AFFECTED BY AIR POLLUTION

Using the pooled estimates of relative risks from our analysis, we estimated that exposure to fine particles at the current ambient level in Canada would lead to

Figure 3: Photographs of air pollution in Montreal and Beijing. Panel A: a "clean" day in Montreal, August 27, 2002, mean concentration of fine particles 3 µg/m3. Panel B: a "dirty" day in Montreal, August 14, 2002, mean concentration of fine particles 37 µg/m3. Panel C: a "clean" day, in Beijing, mean concentration of respirable particles 3 µg/m3; Panel D: a "dirty" day, in Beijing, mean concentration of respirable particles 254 µg/m3

approximately 5,000 deaths each year nationwide (66). Among these deaths, 1,100 deaths would be from lung cancer and 2,700 deaths would be from cardiovascular diseases. In fact, it has been reported that for Austria, France, and Switzerland combined, 40,000 deaths per year are likely to be attributable to outdoor air pollution (67). Chronic health effects from exposure to urban air pollution have thus been estimated to account for almost 60% of the total environmentally-related health effects, exceeding the effects from other environmental risk factors, such as environmental tobacco smoking and lead contamination in drinking water (68).

BIOLOGICAL MECHANISMS

The mechanisms by which air pollution influences the risk of cardiovascular disease are still under investigation. Most of the research in the past 15 years has been focused on the effects of particulates despite the evidence of associations for other pollutants, especially for acute effects. In any event, several potential pathophysiological pathways for the effects of particles have been suggested (18;69). First, repeated inhalation of ambient particulates may result in low-to-moderate-grade pulmonary oxidative stress and inflammation (70-73), which subsequently triggers systemic inflammatory responses with a cascade of reactions: production and mobilization of proinflammatory leukocytes and platelets into the circulation (74;75); increase in circulating inflammatory mediators, such as interleukins (IL)-6 (76;77); and stimulation of the production of acute phase proteins, such as C-reactive protein and fibrinogen (70). This induced systemic inflammatory response may in turn lead to increasing blood coagulability, accelerating atherosclerosis progression, and ultimately precipitating or aggravating cardiovascular events (78-80). This possible biological mechanism, proposed by Seaton et al. (79) and van Eeden et al. (80), has been supported by accumulated epidemiological evidence (67;81) that exposure to ambient fine particles is positively associated with development of atherosclerosis. Second, it has been hypothesized that sustained inflammation of the lung may also exacerbate pre-existing lung diseases such as chronic obstructive pulmonary disease, which further contributes to cardiovascular risk (82). A third hypothesized pathophysiological pathway suggests that ultrafine particles and soluble components of fine particles may cross the pulmonary epithelium into the circulation, thus conferring a direct effect on the cardiovascular system by altering cardiac autonomic function: perhaps contributing to the instability of a vascular plaque or initiate cardiac arrhythmias (18;69). There is evidence that decreases in resting heart rate, an

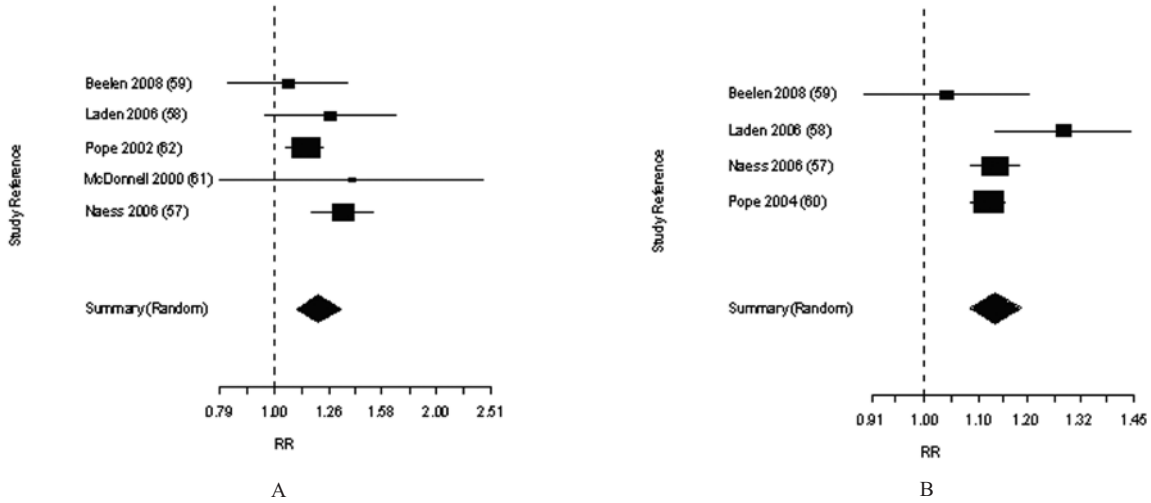

Figure 4: Meta-analysis of epidemiological studies (1950-2007) of the association between long-term exposure to fine particles and mortality from lung cancer (A) and of the association between long-term exposure to fine particles and overall cardiovascular mortality (B). [For each study (shown by last name of first author, year of publication, and reference number), the rectangular box represents the size of study population, the center of the box denotes the point estimate of the relative risk, and the horizontal bar indicates 95%CI of the relative risk. The diamond symbol depicts the summary estimate of the relative risks using a random effects modeling. RR denotes relative risk]

indicator of cardiac autonomic function, are associated with increased risk of cardiovascular morbidity and mortality in the elderly and those with heart disease (83;84). This latter pathway may explain both the acute and the long-term cardiovascular effects of particulate pollution.

In contrast, it appears that the gaseous pollutants may not play a great role in carcinogenesis because they are not mutagenic. Although urban air also contains volatile organic compounds (e.g., benzene) and polycyclic aromatic hydrocarbons (e.g., benzo[a]pyrene) that are both mutagenic and carcinogenic (21), most of these compounds have not been investigated in population-based epidemiological studies. The biological mechanisms underlying the association between fine particles and lung cancer have not been elucidated. It is hypothesized that lung cancer develops through a series of progressive pathological changes occurring in the respiratory epithelium as a result of direct genotoxicity effects of particulate air pollution (85;86). Some studies have suggested that urban air pollution, in particular polycyclic aromatic hydrocarbons, may cause cancer mediated through the formation of DNA adducts (87-90). Polycyclic aromatic hydrocarbons can adhere to fine particles (91). Indeed, it was found that more than 90% of the particulate phase of polycyclic aromatic hydrocarbons are associated physically with particulates under 3.3 μm (92).

CONCLUSIONS

Air pollution does not recognize national boundaries and it may be transported over distances of thousands miles (20). Even at its current level, air pollution threatens the health of entire populations. Air pollution is a growing, global problem. Yet approaches to controlling air pollution have not been up to the task. The overall evidence from the past and present epidemiological studies strongly supports tighter standards for air pollution, especially particulate pollutants, in Canada and in other countries.

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FOCUS REVIEW

Beyond the News: Health Risks of Climate Change

Kristie L. Ebi*

INTRODUCTION

Climate change is affecting the health of millions of people through altering the geographic distribution and incidence of climate-sensitive health outcomes, including through injuries, illnesses, and deaths due to extreme weather events, food-, water-, and vectorborne diseases, air pollution, aeroallergens, and malnutrition (1). The magnitude of impacts is projected to increase as the climate continues to change. The scope and scale of projected impacts mean that climate change will touch the professional and personal lives of many public health and health care professionals. Avoiding, preparing for, and effectively responding to the health risks of climate change will require broad engagement of scientists, decision-makers, and the public. Achieving this engagement means that increased scientific literacy is needed of the causes and implications of climate change for human health.

There are growing numbers of assessments of the potential health impacts of climate change (1-4) and summaries for various audiences (5). Instead of summarizing current knowledge of the causes and consequences for human health of anthropogenic climate change, this paper will highlight a few issues that may help with understanding the human health impacts of climate change.

Energy drives climate change as well as its consequences

Energy refers to both the energy derived from burning fossil fuels, which, along with deforestation, is the primary cause of anthropogenic climate change, and to the resulting increased energy within the climate system that is manifest in the form of increased temperatures, alterations of the hydrologic cycle, and more frequent and intense extreme weather events.

The principal driving force for weather and climate is the uneven warming of the Earth's surface (due to the angle of rotation). Complex and changing atmospheric and oceanic patterns redistribute the absorbed solar energy from the equator to the poles. In addition, some absorbed energy is reradiated as long-wave (infrared) radiation. Some of this infrared radiation is then absorbed by the atmospheric greenhouse gases (including water vapour, carbon dioxide, methane, nitrous oxide, halocarbons, and ozone) and reradiated back to the Earth, thereby adding additional energy to the atmosphere and oceans. This greenhouse effect warms the surface by more than would be achieved by incoming solar radiation alone and raises the global average surface temperature to its current 15°C (6). Without this warming, the Earth's diurnal temperature range would increase dramatically, and the global average surface temperature would be about 33°C colder. Increasing concentrations of greenhouse gases are increasing the energy in the atmosphere, further warming the planet.

Current concentrations of atmospheric CO_2 and ethane far exceed pre-industrial values found in polar ice core records dating back 650,000 years; the concentration of atmospheric CO_2 has increased from a pre-industrial value of about 280 ppm to 379 ppm in 2005 (7). Since 1750, it is estimated that about 2/3rd of anthropogenic CO_2 emissions have come from fossil fuel burning and about 1/3rd from land use change. Ambient temperatures increased 0.74°C worldwide over the period 1906-2005. The rate of warming averaged over the past 50 years (0.13°C + 0.03°C per decade) is nearly twice that for the last 100 years (Figure 1), and at least six times faster than at any time during the 2,000 years.

The Earth is committed to decades of climate change

Figure 2, from the Intergovernmental Panel on

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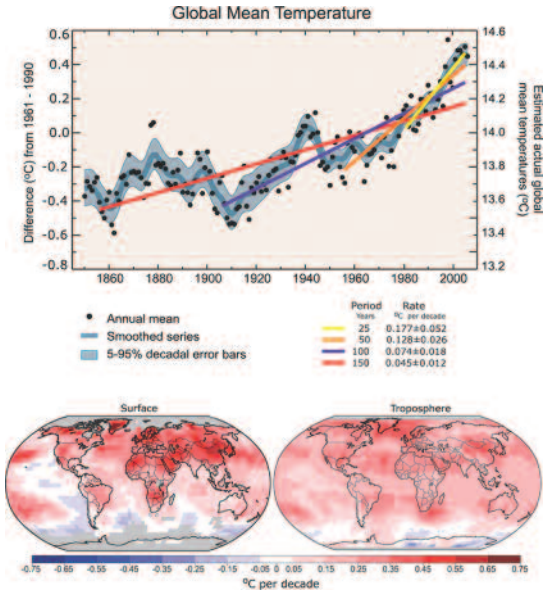

Figure 1: Figure 1: Global mean temperature increase (°C) from 1850 to 2005 (7). Annual global mean temperatures (black dots) with linear fits to the data. The left axis shows temperature anomalies relative to 1961-1990 and the right hand axis shows estimated actual temperatures. Linear trends are shown for the last 25 (yellow), 50 (orange), 100 (magenta), and 150 (red) years. The smoothed blue curve shows decadal variations. The total temperature increase from the period 1850 to 1899 to the period 2001 to 2005 is 0.76°C + 0.19°C.

Climate Change (IPCC), shows projected temperature changes over this century based on different scenarios of greenhouse gas emissions (7). These scenarios are based on differing assumptions of future demographic, economic, and technology changes that determine the amount of fossil fuels that will be burned. The IPCC projected that the global mean temperature of the Earth would increase by the end of the 21st century by between 1.1 and 6.4°C (7). This projected rate of warming is much larger than the observed changes during the 20th century and is very likely to be without precedent during at least the last 10,000 years.

The orange line on the figure is the climate change commitment or the amount of warming that will occur no matter the degree to which greenhouse gas emissions are reduced over the next few decades. This commitment is due to the inherent inertia in the climate system. Natural processes currently remove about half the incremental anthropogenic CO2 added to the atmosphere annually; the balance is removed over one to two hundred years (7). The Earth is committed to nearly as much warming as has already occurred.

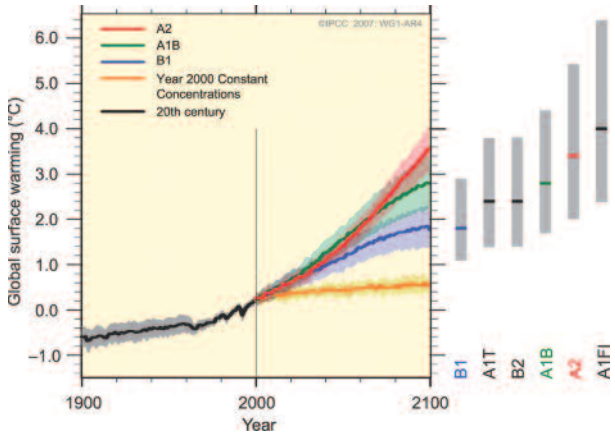

Figure 2: Observed and Projected Global Mean Surface Temperatures (°C), 1900 to 2100. Solid lines are multi-model global averages of surface warming (relative to 1980–1999) for the scenarios A2, A1B and B1, shown as continuations of the 20th century simulations. Shading denotes the ±1 standard deviation range of individual model annual averages. The orange line is for model runs where concentrations were held constant at year 2000 values. The grey bars at right indicate the best estimate (solid line within each bar) and the likely range assessed for the six SRES (Standardized Reference Emission Scenarios) marker scenarios.

Climate change is about changes in long-term averages as well as extremes

Climate change will increase both temperatures and climate variability. Assuming a normal distribution of surface temperature, climate change could increase mean temperature without a change in the variability (e.g. the shape of the curve would remain the same but would be shifted towards warmer temperatures); increase the variability without a change in mean temperature (e.g. the shape of the curve would become flatter, thus increasing the number of both hot and cold weather extremes); or shift both the mean and the variability of temperature, which would result in slightly less cold weather and substantially more hot and record hot weather. There is growing concern that

Standardized Reference Emission Scenarios

Standardized Reference Emission Scenarios (SRES) were developed by the Intergovernmental Panel on Climate Change as alternative images of how the future might unfold.12 Four different narrative storylines were developed to describe the relationships between greenhouse gas emission driving forces and their evolution. Probabilities or likelihood were not assigned to the individual scenarios. There is no single most likely, or best guess, scenario. None of the scenarios represents an estimate of a central tendency for all driving forces or emissions.

Each SRES storyline assumes a distinctly different direction for future development, such that the four storylines differ in increasingly irreversible ways. The storylines were created along two dimensions – global vs. regional development patterns and whether economic or environmental concerns would be primary. It is important to note that the scenarios do not cover all possible future worlds. For example, there is no SRES world in which absolute incomes are constant or falling. The A2 and B2 storylines are frequently used in modeling health impacts.

The A2 storyline describes a very heterogeneous world with an underlying theme of self-reliance and preservation of local identities. Fertility patterns across regions vary slowly, resulting in continuously increasing global population. Economic development is primarily regionally oriented and per capita economic growth and technological change are fragmented and slower compared with the other scenarios.

The B2 storyline describes a world in which the emphasis is on local solutions to economic, social, and environmental sustainability. It is a world with continuously increasing global population (at a rate slower than A2), intermediate levels of economic development, and less rapid and more diverse technological change.

future weather patterns will resemble this last pattern and that what is currently considered an extreme event may become common.

The IPCC concluded that climate change has already increased the frequency, intensity, and duration of some extreme weather events (Table 1) (7). This increase in extremes is expected to accelerate with additional climate change, and will have obvious implications for human health.

The future will not be like the past

A main consequence of climate change for human societies is that the future will not be like the past. Most of our infrastructure was built assuming that the weather in the next few decades will pretty much be like the weather today, resulting in hospitals, power plants, and other critical infrastructure in some regions now lying in flood plains and along coastal regions where sea level rise and storm surges put them at risk of inundation. Changing climatic patterns also are not taken into consideration in critical public health and health care programs, such as surveillance and control activities.

Research is documenting climate change impacts on the atmosphere, oceans and biosphere on which human health and well-being depend (7). Few health organizations and agencies explicitly incorporate the potential risks of and responses to climate change into their programs and activities. Increasing mortality from heatwaves and other extreme weather events, changes in the geographic range and incidence of climate-sensitive infectious diseases, increasing morbidity and mortality from poor air quality, and other health impacts will require modification of current public health programs (8,9) and training of health care providers to be prepared for patients presenting with currently unexpected climate-sensitive health outcomes (5).

Health impacts will depend on the local context

The causal chain from climate change to changing patterns of health determinants and outcomes is complex and includes factors such as wealth, distribution of income, status of the public health infrastructure, and access to medical care (10). Therefore, the severity of future impacts will be determined by changes in climate as well as by concurrent changes in nonclimatic factors. This means that impacts will vary by location; one exposure-response relationship may not explain observed impacts across regions or across vulnerable groups. One key determinant of the extent of impacts is the status of the public health infrastructure. For example, Fleury et al. (11) found strong non-linear associations between ambient temperature and the occurrence of Salmonella, pathogenic Escherichia coli, and Campylobacter in Alberta. In Newfoundland-Labrador, a relationship was found only for Campylobacter. The number of additional cases due to climate change can be projected, assuming the relationships remain the same with higher temperatures. However, the number of additional cases

Phenomenon and Direction of Trend	Likelihood that trend occurred in 20th Century	Likelihood of a Human Contribution to Observed Trend	D	Likelihood of Future Trend Based on Projections for 21st Century
Warmer and fewer cold days and nights over most land areas	Very likely	Likely	*	Virtually certain
Warmer and more frequent hot days and nights over most land areas	Very likely	Likely (nights)	*	Virtually certain
Warm spells / heatwaves: frequency increases over most land areas	Likely	More likely than not		Very likely
Heavy precipitation events: frequency (or proportion of total rainfall from heavy falls) increases over most areas	Likely	More likely than not		Very likely
Area affected by droughts increases	Likely in many regions since 1970s	More likely than not	*	Likely
Intense tropical cyclone activity increases	Likely in many regions since 1970s	More likely than not		Likely
Increased incidence of extreme high sea level	Likely	More likely than not		Likely

Table 1: Recent Trends, Assessment of Human Influence, and Projections of Extreme Weather and Climate Events for Which There is Evidence of an Observed Late-20th Century Trend (7).
*An asterisk in column D indicates that formal detection and attribution studies were used, along with expert judgment, to assess the likelihood of a discernible human influence.

Climate-Sensitive Health Outcome	*Particularly Vulnerable Groups*
Heat-related illnesses and deaths	Elderly, chronic medical conditions, infants and children, pregnant women, urban and rural poor, outdoor workers
Diseases and deaths related to air quality	Children, pre-existing heart or lung disease, diabetes, athletes, outdoor workers
Illnesses and deaths due to extreme weather events	Poor, pregnant women, chronic medical conditions, mobility and cognitive constraints
Water- and foodborne illness	Immunocompromised, elderly, infants
Vectorborne illnesses	
Lyme disease	Children, outdoor workers
Hantavirus	Rural poor, occupational groups
Dengue	Infants, elderly
Malaria	Children, immunocompromised, pregnant women, genetic

Table 2: Climate-Sensitive Health Outcomes and Particularly Vulnerable Groups (2).

actually experienced will depend on the effectiveness and timeliness of additional public health interventions to reduce cases of enteric disease.

Not everyone is equally vulnerable to the health risks of climate change

Sub-populations that are most vulnerable to the health impacts of climate change depend on the region, the health outcome, and population characteristics, including human, institutional, social, and economic capacity (8). Individual vulnerability depends on genetic, developmental, acquired, and socioeconomic factors. In general, the most vulnerable include children, older adults, those with chronic medical conditions, socially disadvantaged individuals, those living in water-stressed and coastal and low-lying areas, and populations highly dependent on natural and resources. Table 2 summarizes vulnerable populations by health outcome.

Public health and health care systems need to be strengthened

Responsibility for the prevention of climate-sensitive health risks rests with individuals, community and state governments, national agencies, and others. The primary response in most cases will be to strengthen current programs and activities to reduce the burden of climate-sensitive health outcomes, such as improving food-, water-, and vectorborne disease surveillance programs (8,9). In some cases, programs will need to be implemented in new regions; in others, climate change may reduce current infectious disease burdens. The degree to which programs and measures will need to be augmented to address the additional pressures caused by climate change will depend on factors such as the current burden of climate-sensitive diseases; the effectiveness of current interventions; projections of where, when, and how the burden of disease could change with changes in climate and climate variability; the feasibility of implementing additional cost-effective interventions; other stressors that could increase or decrease resilience to impacts; and the social, economic, and political context within which interventions are implemented (8). Strengthening health systems will enable them to deal with both gradual changes in climate as well as sudden impacts (such as extreme weather events).

Future climate change will depend on the choices made in the next few years

As mentioned previously, Figure 2 shows projected temperature changes over this century based on different scenarios of greenhouse gas emissions (7). The scenarios include future demographic, economic, and technology changes that determine the amount of fossil fuels that will be burned. All of these changes are the result of human choices, including individual and collective choices related to energy efficiency, as well as national choices on investments in technology. Because of the inertia in the climate system, the choices made in the next few years will affect the rate and magnitude of climate change for our children and grandchildren.

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FOCUS REVIEW

Does Exposure to Agricultural Chemicals Increase the Risk of Prostate Cancer among Farmers?

Marie-Élise Parent*, Marie Désy, and Jack Siemiatycki

ABSTRACT: Several studies suggest that farmers may be at increased risk of prostate cancer. The present analysis, based on a large population-based case-control study conducted among men in the Montreal area in the early 1980's, aim at identifying occupational chemicals which may be responsible for such increases. The original study enrolled 449 prostate cancer cases, nearly 4,000 patients with other cancers, as well as 533 population controls. Subjects were interviewed about their occupation histories, and a team of industrial hygienists assigned their past exposures using a checklist of some 300 chemicals. The present analysis was restricted to a study base of men who had worked as farmers earlier in their lives. There were a total of 49 men with prostate cancers, 127 with other cancers and 56 population controls. We created a pool of 183 controls combining the patients with cancers at sites other than the prostate and the population controls. We then estimated the odds ratio for prostate cancer associated with exposure to each of 10 agricultural chemicals, i.e., pesticides, arsenic compounds, acetic acid, gasoline engine emissions, diesel engine emissions, polycyclic aromatic hydrocarbons from petroleum, lubricating oils and greases, alkanes with ≥18 carbons, solvents, and mononuclear aromatic hydrocarbons. Based on a model adjusting for age, ethnicity, education, and respondent status, there was evidence of a two-fold excess risk of prostate cancer among farmers with substantial exposure to pesticides [odds ratio (OR)=2.3, 95% confidence interval (CI) 1.1-5.1], as compared to unexposed farmers. There was some suggestion, based on few subjects, of increased risks among farmers ever exposed to diesel engine emissions (OR=5.7, 95% CI 1.2-26.5). The results for pesticides are particularly noteworthy in the light of findings from previous studies. Suggestions of trends for elevated risks were noted with other agricultural chemicals, but these are largely novel and need further confirmation in larger samples.

INTRODUCTION

Prostate cancer is the most frequently occurring cancer among Canadian men.(1) Despite extensive research, the etiology of this disease remains poorly understood. Only a few risk factors for prostate cancer have been clearly established to date including age, a positive family history of the disease, and ethnicity. The normal function of the prostate is controlled by testosterone, and androgenic stimulation of the prostate over a prolonged period may promote or initiate carcinogenesis.(2,3) The prostate gland is also sensitive to estrogens.(4) Administration of estrogens reduces testosterone production, and is used to control disseminated prostate cancer. However, there is epidemiologic and experimental evidence suggesting that estrogenic hormones may cause DNA damage and initiate prostate cancer.(5-9) Taken together, these observations suggest that both androgens and estrogens are associated with the risk of prostate cancer, and that exogenous factors that could influence hormone levels could play an etiological role. The large gradients in risks across ethnic groups, geographical areas and the evidence from migrant studies point out to a strong, as yet undefined, influence of environmental factors.(10) It is thought that prostate cancer could result from a complex interplay between several environmental, lifestyle and genetic factors. (10-13)

The possible etiologic role of environmental factors, such as those encountered in the workplace, has been

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reviewed.(12) A large number of studies have assessed the risk of prostate cancer in various occupation groups. Most of them were based exclusively on job titles, providing only indirect evidence of the underlying risk factors. There are some hints that occupational groups potentially exposed to pesticides, which include farmers but also pesticide manufacturers, workers exposed to metalworking-related substances, workers exposed to diesel engine emissions, to polycyclic aromatic hydrocarbons (PAH) and to cadmium might experience excess risks. The evidence is reviewed briefly here.

Farming, pesticides and herbicides: One puzzling observation is the generally consistent pattern for an excess risk of prostate cancer among farmers.(12) At least 100 studies have examined the relationship between farming (as a job title) and prostate cancer. Results from meta-analyses based on these are consistent with a weak, positive association.(14-17) However, with a summary relative risk of about 1.1, chance cannot be ruled out with certainty. The association might also reflect some systematic bias, possibly publication bias. Finally the positive association might reflect lifestyle factors or environmental factors such as occupational exposures. The slight excess of prostate cancers contrasts with low risks for most other cancers and non-neoplastic diseases among farmers.(14) The interpretation of this body of evidence remains uncertain.(18)

Very few studies to date have considered, other than in a very crude way, the role of specific chemical agents in the farmers' environment. Because several pesticides are estrogen-like compounds that can modulate hormone levels,(19) these agents are under particular suspicion. Yet the evidence for a putative role of pesticides in prostate cancer etiology is still very limited. Use of pesticides has been associated with prostate cancer in some(20-27) but not all studies.(28-32) Discordant evidence concerning hazards due to pesticides also comes from studies of workers involved in manufacturing or spraying of these compounds(33-42), and pesticide applicators.(4,43-55) Most of these studies were quite small. Early reports from the Agricultural Health Study Cohort regarding chlorinated pesticides are conflicting.(56,57) Finally, in a few studies,(58,59) but not all,(23,25,29,60) elevated risks for workers exposed to fertilisers have been reported. Genetic susceptibility might modify prostate cancer risk from pesticide exposure.(61,62)

Farming can involve a wide range of activities, including equipment operating, mechanical maintenance and repair, soldering, carpentry, livestock handling, pesticide, fertilizer application, etc. These can entail potential exposures to very diverse agents such as solvents, fuels and oils, metal dusts, welding fumes, engine exhausts, paints, pesticides, herbicides, insecticides, fertilizers, zoonotic viruses, microbes, fungi, organic dusts, and sunlight. For most of these, evidence with regard to prostate cancer is lacking.

Metalworking-related exposures: Metal workers such as mechanics, repairmen, and machine operators may be at increased risks of prostate cancer.(63-65) However, in few studies were specific exposures examined. Among those that did, there was some evidence of associations with some metallic dusts and with metalworking chemicals, such as solvents, cutting oils, mineral oils, heating oils, hydraulic fluids, lubricating oils and acids.(64,66-69) These findings were not always replicated, however.(32)

PAH and engine emissions: There is some evidence, albeit not entirely consistent,(70) of excess risks in occupational groups with potential exposure to PAHs.(66,71-77) In a few studies that entailed substance-based exposure assessment protocols, one found excess risks in relation to liquid fuel combustion products and PAH as a class,(66) and another(78) found excess risk in relation to diesel fuel and fumes, soot, tar and pitch. Contrasting results, suggesting no association with PAHs or diesel fumes, have been reported as well.(32,67) Diesel engine emissions may induce changes in enzymatic activities in the prostate glands of animals.(78,79) In addition, the anti-estrogenic effects of certain hydrocarbons, such as benzo(a)pyrene, may promote the growth of prostate cancer cells. Several PAHs may interact with estrogen receptor signalling.(80)

Cadmium: Cadmium is found in some insecticides and fertilisers, and exposure can occur in several workplaces. Other sources include diet and tobacco smoke.(77) Following some early reports of excess risk of prostate cancer among cadmium-exposed workers, more recent and larger studies failed to confirm these.(81-83) Nevertheless, experimental data suggest that prostatic tumours can be induced experimentally in rodents by oral exposure to cadmium.(84)

Overall, the available evidence on occupational factors remains limited. The vast majority of studies of occupational circumstances and prostate cancer conducted to date were retrospective mortality studies in which job or industry titles as recorded on death certificates were used as indices of exposure. Although such studies are useful in providing leads, what is really needed are studies of occupational factors based on refined exposure assessment protocols.(18,85)

One of the most detailed and in-depth evaluations of the association between occupational exposures and prostate cancer has been carried out by our research group through analyses of our multiple-site, case-control study conducted in Montreal in the

1980s.(86,87) Several occupational substances exhibited moderately strong associations with prostate cancer, including metallic dust, liquid fuel combustion products, lubricating oils and greases, and PAH from coal.(66) Estimates of the proportion of prostate cancer cases in the population that would be attributable to occupational exposures ranged from 12 to 21 percent. These figures may have been somewhat overestimated and precision was low. Still, even if the true attributable fraction were in the range of 5 to 10 %, it would represent an important public health issue. Interestingly, we have recently found a similar pattern of risk in relation to prostate cancer for exposure to some of these substances during leisure-time activities.(88)

In order to further investigate the role of agricultural exposures in prostate cancer, we conducted a new analysis of the aforementioned Montreal-based study, this time focusing on men, both cases and controls, with a history of farming. Results from these analyses are reported here.

MATERIALS AND METHODS

Study sample

In the 1980s, our research group undertook a large population-based case-control study in Montreal to explore the relationship between hundreds of occupational exposures and 19 cancer sites. This study has been described in detail elsewhere.(86) Briefly, nearly 4,000 incident cancer cases, all males, were recruited, including 449 prostate cancer patients. A group of 533 population controls, frequency matched on age and residential area to the cancer patients, was also interviewed.

For the purpose of the present analyses, we restricted the case series to those 49 prostate cancer cases who had ever been farmers, and constituted a control series of 183 men who had also been farmers (combining 56 population controls and 127 patients with cancer at a site other than the prostate). No cancer type represented more than 20% of the entire group of 127 cancer patients.

Data collection

Data were collected as part of face-to-face interviews. Information was collected on socio-demographic factors and lifestyle. A semi-structured questionnaire was used to obtain a detailed description of each job held by each subject over his lifetime. Trained interviewers probed for details about work activities, raw material used, work environment, etc. A team of expert chemists and industrial hygienists then reviewed each reported job and inferred the potential exposure to 294 chemical agents.

For each exposure thought to be present in the worker's environment, the team of chemists had to describe the degree of certainty that the exposure actually occurred (whether it was possible, probable or definite), the frequency of exposure (less that 5% of time in a normal work-week, 5 to 30% of time, or more than 30%), the relative concentration of the exposure (low, medium or high), and the number of years of exposure.

Data analysis

Unconditional logistic regression was used to model the risk of developing prostate cancer associated with exposure to the selected chemicals during farming. Potential confounders entered into the regression models included age (years), ethnicity (French / Anglo / Italian / Other European / Other), educational level (years), and respondent status (self / proxy).

Ten chemicals were retained for analysis. Firstly, we selected 4 substances which had at least 20% lifetime prevalence of exposure among controls, and which were either of a priori interest based on studies of occupational groups, i.e., pesticides, diesel engine emissions, PAH from petroleum, and lubricating oils and greases. Secondly, we expanded the list of chemicals to be studied to include 6 other substances who had so-called suggestive odds ratios in this database, defined here as 1.3 or more. These were: arsenic compounds, acetic acid, gasoline engine emissions, alkanes with 18 carbons or more, solvents, and MAH.

Only those subjects categorized as "probably" or "definitely" exposed to the selected agricultural chemicals by the expert chemists/hygienists were considered as exposed. Moreover, we excluded from the analyses those subjects who had been exposed only in the 5 years before diagnosis or enrolment in the study.

We first conducted analyses categorizing subjects as never or ever exposed to the agricultural chemicals under study. For pesticides, for which there were sufficient numbers, we further restricted our analysis to a subset of subjects with "substantial" exposure, defined as having a medium or high frequency of exposure, a medium or high concentration of exposure and a duration of exposure greater than 5 years. Finally, we assessed the risk of prostate cancer associated with increasing concentration, frequency, and duration of exposure to pesticides.

RESULTS

Farmers with prostate cancer were more often of French ancestry than control farmers (Table 1). Cases and controls differed marginally in terms of educational level and respondent status. Seventy nine percent of

Characteristics	Cases	Controls
Mean age (years)	63	61
Ethnicity (%)		
French	78	56
Anglo	2	7
Italian	12	22
Other European	8	13
Other	0	2
Mean educational level (years)	8	7
Proxy respondents (%)	14	17

Table 1. Characteristics of the 49 case farmers and 183 control farmers

farming occupations reported in this study population were as farm workers or farm labourers, while 21% were as farm manager, foreman or owner.

Subjects categorized here as exposed had been exposed only during farming, and never in other jobs held by farmers. There were in fact four substances which were exclusive to farming, namely pesticides, arsenic compounds, acetic acid and diesel engine emissions, which means that they were never encountered in other jobs that the farmers had held.

Table 2 shows the risk estimates for prostate cancer associated with ever exposure to the selected substances. Odds ratios were slightly elevated for all 10 chemicals studied, although only diesel engine emissions achieved statistical significance.

For pesticides (Table 3), we also assessed risks associated with exposure at the substantial level, as well as according to the different dimensions of exposure. Farmers with substantial exposure to pesticides had a significant, two-fold excess in risk, compared to unexposed farmers. The risk increased slightly with increasing frequency and duration of exposure. Nearly all exposures to pesticides were rated at the medium concentration level, precluding an evaluation of the risks with increasing concentration levels.

DISCUSSION

Results from this analysis offer a glimpse at the role of pesticides on the risk of prostate cancer among farmers. One particular characteristic of this study is that it was based on both case and control farmers. Farmers tend to have a specific lifestyle related to their work activities. Nearly all previous studies of farmers and prostate cancer have used non-farmers as controls. Our approach might have made our cases and controls more homogeneous in terms of their lifestyle habits, thereby providing some internal adjustment for potential as yet undefined lifestyle-related risk factors for prostate cancer. However, by doing so, we might have attenuated our chances of observing differences in risks associated with chemical exposures. For this reason, the odds ratios estimated here possibly represent conservative estimates of risk.

Advantages of the study include the detailed exposure assessment scheme, based on expert judgment, carried out on a case-by-case basis, and based on in-person interviews eliciting detailed job description and work practices. This exposure assessment approach is recognized as the reference method for such as study design.(89) Moreover, prostate cancer cases were incident cases, we had access to different control groups, and were able to adjust for some potential confounders.

The main limitation of this analysis is the small number of farmers it is based on, owing to the population-based nature of the study. We had no information on dietary habits. However, because this analysis was restricted to farmers, cases and controls might have been relatively comparable in this respect.

The types of pesticides used were not systematically elicited from the subjects. However, among those who volunteered the information, the most common types were “Paris Green” (a mixture of lead arsenate, acetic acid, and mineral oil), lime (calcium oxide), Dichloro-Diphenil-Tricholoethane, and “Bouillie Bordelaise” (a mixture of copper sulfate and lime).

Investigating prostate cancer risks in relation to occupational exposures is important because exposure levels in the workplace may be higher than in the general environment and because most workplace substances find their way into the general

Exposure	N_{ca}	OR	95%CI
Pesticides	25	1.4	0.7-2.7
Arsenic compounds	15	1.4	0.6-3.0
Acetic acid	12	1.5	0.7-3.4
Gasoline engine emissions	5	1.3	0.4-4.5
Diesel engine emissions	5	5.7	1.2-26.5
Polycyclic aromatic hydrocarbons from petroleum	6	1.4	0.3-5.8
Lubricating oils and greases	9	1.5	0.6-4.0
Alkanes with ≥18 carbons	9	1.8	0.7-5.0
Solvents	7	1.8	0.6-5.6
Mononuclear aromatic hydrocarbons	6	1.7	0.5-5.4

Table 2. Odds ratio (OR)* and 95% confidence interval (CI) for prostate cancer associated with ever exposure to selected chemicals during farming

*Adjusted for age, ethnicity, education, respondent status

environment.(85) Understanding whether occupational chemicals cause prostate cancer is important not only for prevention, but it can also contribute to an understanding of carcinogenesis. While there is still limited physiologic evidence on the extent to which different exogenous chemicals may affect the prostate gland, it is known that some chemicals (i.e., dioxins, diesel emissions) can alter enzymatic activity in the prostate.(79,90) Exposure to certain chemicals such as cadmium can induce prostate tumours in animals.(91)

A great deal of interest is being directed towards the hypothesis that certain environmental chemicals may act as endocrine disruptors or modulators.(2-4,19,92,93) Exposure during development and adult years could be relevant.(94) The effects may be due to their a) mimicking endogenous hormones such as estrogens and androgens, b) antagonising endogenous hormones, c) altering the pattern of synthesis and metabolism of hormones, and/or d) modifying hormone receptors levels. As hormonal influences are likely related to prostate cancer etiology, hormone-modulating exogenous chemicals are of particular interest.(95) Several industrial chemicals have been associated with endocrine-disrupting effects including some metals (cadmium, lead, mercury, aluminium), phenolic derivatives (phenol, bisphenol-A, pentachlorophenol, resorcinol, PCBs), phthalates (used as plasticizers), variously substituted benzenes (polycyclic aromatic hydrocarbons [PAH], benzo[a]pyrene), styrenes (used in the manufacture of plastics and rubber), carbon disulphide (used in the production of rayon), dioxin, and several organochlorine pesticides, fungicides and herbicides.(93,96-100) Extremely low exposures to some endocrine modulators (plasticizers, alkylphenols) have been found to induce adverse effects on the male reproductive tract of rodents.(100) Considerable concentrations of chlorinated hydrocarbons can accumulate in the male genital tract, in the reception zone for spermatozoa.(101) Also, endogenous estrogens are bound to the sex hormone-binding globulin while many exogenous estrogens are not, resulting in higher concentrations of free compounds.(19) Taken together, this body of evidence suggests that exposure to a wide variety of exogenous chemicals would modulate hormone levels, which in turn, could influence prostate cancer development.

Pesticides	N_{ca}	OR	95%CI
Level of exposure			
Any	25	1.4	0.7-2.7
Substantial	17	2.3	1.1-5.1
Frequency of exposure			
Low	7	0.9	0.3-2.3
Medium or high	18	1.7	0.8-3.6
Duration of exposure			
Up to 10 years	11	1.2	0.5-2.8
More than 10 years	14	1.5	0.7-3.4

Table 3: Odds ratio (OR)* and 95% confidence interval (CI) for prostate cancer associated with exposure to pesticides during farming by level, frequency and duration of exposure

*Adjusted for age, ethnicity, education, respondent status

CONCLUSION

In conclusion, farmers exposed to high levels of pesticides had a two-fold excess risk of prostate cancer compared to unexposed farmers. Exposure to diesel engine emissions was also associated with elevated risks, but statistical precision was low. Hints of excess risks were noted for other chemicals. Some of these tended to be correlated to one another, which would explain why risk estimates were similar for several of the chemicals studied. For instance, arsenic compounds and acetic acid are common ingredients in some pesticides. Conversely, activities involving agricultural machinery repairs would be expected to entail conjoint exposure to several chemicals such as lubricating oils and greases, solvents and engine emissions.

The results presented here are based on a limited sample. Nevertheless, in light of the accruing epidemiological and experimental evidence, further exploration around these potential associations is warranted. The Agricultural Health Study, a US-based prospective cohort study initiated in 1993, currently follows a large group of pesticides applicators from Iowa and North Carolina. It is hoped that upcoming results from this large study will shed light on the health risks, including prostate cancer, incurred by agricultural workers.

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FOCUS REVIEW

Climate Change and Health in Canada

Lea Berrang Ford*

INTRODUCTION

National governments from around the world met in Poznan, Poland in December 2008 at the 14th Conference of the Parties to the United Nations Framework Convention on Climate Change (1). This conference came at a time of increasing political and scientific confidence in the role of human-induced greenhouse gas emissions in changing global temperatures. The most recent (2007) report of the Intergovernmental Panel on Climate Change (2) states that climate change is now "unequivocal", based on increasing evidence from global average air and ocean temperatures, melting of snow and ice, and rising global average sea level" (2). While there remains uncertainty regarding the specific nature and rate of climatic changes and their impacts, there is negligible scientific doubt that the global climate is changing and that these changes will have significant and potentially profound impacts on a wide range of ecological and human systems across the planet (3-6).

That climate change predictions are both scientifically and politically daunting lessens neither their verity nor implied imperative (7, 8). Climate change will involve an average increase in global temperatures of approximately 1.1-6.4°C by the end of the century (1); this range reflects both uncertainty in climate modeling, as well as a range of possible scenarios for how we will respond to climate changes, including mitigation, technology development, economic development and population growth. This temperature shift will be manifest in average global climatic changes, including higher maximum temperature, more very hot days, increased occurrence and severity of heat waves, fewer cold and frost days, fewer cold spells, more intense precipitation events, increased risk of drought in continental areas, increased cyclone intensities, and intensified ENSO events. These effects will, however, vary significantly by region and act within existing climate conditions. For example, while parts of Latin America will see minimal changes in temperature, Arctic regions are expected to experience an average temperature shift of 4-7°C by the end of the century (9) and recent research suggests that even these projections may be conservative (6, 10).

Changes in our global and regional climate systems will have important implications for health and health systems (11-22). The World Health Organization estimated that in the year 2000, climate change caused approximately 150,000 excess deaths worldwide, as well as 5 million disability-adjusted life years (19). Temperature and weather have direct effects on mortality and morbidity through the occurrence of extreme weather events, including heatwaves, cold periods, storms, floods, and droughts (11, 23-25). Such events can, in turn, affect the incidence of food-borne and water-borne disease (26, 27). The habitat and survival of insect species capable of transmitting many vector-borne diseases are affected by temperature and water regimes (28, 29). Many pathogen replication cycles are also determined by temperature conditions. Indirect impacts of climate change on livelihoods, such as increased economic vulnerability, reduced availability of food resources, and reduced allocation of government funding for health systems, may also have important, though unquantified, impacts on global health systems (2, 12, 14, 18, 20, 30).

Health impacts due to climate change have already been documented, including changes in the range of some vector-borne diseases (28, 29, 31-33) and an increase in heatwave-related deaths (11, 34, 35). Indirect effects will also include increases in regional food insecurity, migration resulting from environmental degradation, and loss of environmental-dependent livelihoods resulting from ecological shifts in weather or species distributions (16). Table 1 summarizes the reported and projected health impacts of climate change documented by the Intergovernmental Panel on Climate

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Change (IPCC). The IPCC, an intergovernmental body open to all United Nations member countries, comprehensively assesses existing literature related to climate change science, potential impacts, and options for adaptation and mitigation. The published reports represent the consensus of thousands of scientists around the world contributing as authors and reviewers, as well as political consensus required by member countries for the acceptance, adoption and approval of the final document. These projections and measures of confidence are therefore believed to be conservative (3-5).

Current climate change effects on global health are small but increasing in most countries (16). This is due to the lag effect between greenhouse-gas emissions, climate system warming, and the weight of evidence documenting health impacts. While the burden of negative health impacts will be disproportionately high in poorer countries, even high-income countries will be vulnerable to morbidity and mortality related to increases in the number and severity of extreme weather events such as storms, heatwaves, and floods (16). Vulnerable populations in all countries include the urban poor, the elderly and children, traditional communities, subsistence farming communities, and coastal populations (16, 21, 36-38). Evidence does not support the potential for economic development to combat the health impacts of climate change (16).

CLIMATE CHANGE AND HEALTH IN CANADA

Canada will not be immune to the health impacts of climatic change (39-42). Canada has observed approximately 1°C rise in temperature since the beginning of the century, and we can expect this to continue by about 0.5 degree per decade, up to 5°C over the next century (42). This temperature change is not insignificant; the earth's temperature was, for example, only 4-5 degrees cooler during the last ice age (43).

The effects of climate change in Canada will differ between regions (42). While the Prairies are expected to experience warmer, drier summers and more sever summer droughts, Ontario and Quebec can expect decreased snow, increased rainfall, and an increase in the incidence of severe summer storms (44). The greatest changes will occur in the Canadian North, where temperature changes are projected to be among the highest in the world, and where traditional, resource-dependent communities are considered highly vulnerable (9, 42, 45, 46). Indeed, for northern Inuit communities, climate change poses a significant threat to traditional livelihoods in the short to medium term (45, 47-49).

Canada will experience a number of significant direct and indirect impacts of climate change (39-42). Extreme heat events are expected to become more frequent, longer in duration, and more intense (42). Extreme heat events can exacerbate health conditions, such as asthma, as well as lead to an increased number of deaths (11, 23, 50, 51). Heat waves were responsible for over five hundred deaths in Chicago during a 5-day

Existing impacts	**Level of uncertainty ***
Alter the distribution of some infectious disease vectors	Medium confidence
Alter the seasonal distribution of some allergenic pollen species	High confidence
Increase heatwave-related deaths	Medium confidence
Projected impacts	
Increase in malnutrition and consequent disorders, including child growth and development	High confidence
Increase in morbidity and mortality related to heatwaves, floods, storms, fires, and droughts	High confidence
Continued changes in the ranges of some infectious disease vectors	High confidence
Mixed effects on malaria incidence and distribution (expansion in some areas, contraction in others)	Very high confidence
Increase in the burden of diarrhoeal diseases	Medium confidence
Increase in cardio-respiratory morbidity and morality associated with ground-level ozone	High confidence
Increase in the number of people at risk of dengue	Low confidence
Health benefits include fewer deaths due to cold	High confidence

Table 1: Summary of the health impacts of climate change, based on the Intergovernmental Panel on Climate Change Assessment Report Four (16).
* Degree of confidence in being correct: Very high confidence >9 out of 10 chance; High confidence ~8 out of 10 chance; Medium confidence ~ 5 out of 10 chance; Low confidence ~ 2 out of 10 chance (16).

period in 1995 (52) and at least 50,000 deaths in Europe in 2003 (53). Children and the elderly are particularly vulnerable during heat wave events (54). The increasing number of summer days in urban areas of Quebec and Ontario declared unsafe for outdoor activity due to smog and heat can be expected to negatively impact public health through reduced outdoor and exercise activities (55). Poor air quality, resulting from smog and air pollution, is associated with asthma, chronic respiratory disease and cardiovascular disease, and is a serious public health issue in Canada. Smog and air pollution are expected to continue to increase with climatic change (23, 56). Toronto public health recently predicted that climate change would cause a 20% increase in air-pollution related deaths in the city by 2050 (57).

Many regions are expected to see an increase in summer storms. This may affect risks associated with flooding, and will have implications for water quality and contamination (26, 58-60). A prolonged drought followed by a high rainfall event – such as a summer storm – can pick up surface contaminants and flush them into local waterways, causing a 'pulse' in the contaminant load of local water treatment facilities (26, 40). This scenario was determined to be one of the factors contributing to the E. coli outbreak in Walkerton, Ontario in 2000 (61). In addition, higher than normal rainfall events may exceed expected norms for sewage treatment facilities, overwhelming treatment systems. In the Inuit community of Arctic Bay, increased rainfall has been observed to overflow the local sewage ponds, contaminating the bay and roads (62). These scenarios are consistent with climate change predictions and can be expected to occur more frequently.

The distribution of vector-borne diseases will change (40, 41, 63-65). Warmer and wetter summers will affect the distribution and survival of pathogens and some disease vectors such as mosquitoes and ticks (39, 66-68). Research has already documented possible shifts in the distribution of the vector of Lyme disease (29, 69-71), and possible expansion of the potential range of West Nile virus (WNV) (40, 41, 72). Mosquito vectors of WNV will be affected by longer summers (40, 41). Increased incidence of the virus coincides with periods of prolonged hot weather and increased mosquito activity (73). Recent research also indicates the potential for the re-emergence or emergence of exotic pathogens to Canada, including locally-transmitted malaria (63). Emergent disease risks are by nature difficult to predict. Despite this, it is sensible to anticipate the spread of known diseases into new areas and the emergence of new diseases.

There will also be a number of indirect effects on Canadian health and health care. In many cases, these indirect pathways are difficult to identify, predict, and quantify, but may nonetheless be important for changing health systems in Canada. For example, changing sea temperatures are likely to impact the distribution and availability of fish and tree species through impacts on local weather, affecting the viability or focus of fisheries and forestry industries, and by extension the community health and well-being of resource-dependent communities. In this case, the concern is not the loss of traditional species per se – new species are likely to emerge to fill changing niche conditions – but the rate of change in ecological systems, and the ability of industries and communities to adapt to these changes. Similarly, the dramatic spread of the pine beetle has been facilitated – and many suggest triggered – by increasingly favourable weather conditions (74-77). As in the case of the pine beetle, many of the impacts of climate change on health in Canada are likely to be the result of indirect causal processes, and in some cases unforeseen events.

The implications of climate change for health are not limited to global and national impacts. They will also be manifest at the municipal level (Table 2) and within Canada's health sector (41, 55, 78). For Canada's health system, this will result in changing risks. For example,

Sector	Health determinants
Social	Social status
	Social support networks
Economic	Income
	Employment
	Working conditions
Environmental	Air quality & air pollution
	Drinking water quality
	Recreational water quality
	Water availability
	Food safety & inspection
	Regional parks
	Environmental planning & impact analysis
Infrastructure and local works	Housing
	Indoor air quality
	Vector-control
	Land use planning & urban development
	Water distribution, recycling & disposal
	Sewage treatment & inspection
Transport	Public transportation
	Transportation systems and road works
Emergency response	Emergency & disaster preparedness
	Outbreak investigation

Table 2: Health determinants affected by climate change

the increased emergence of new, re-emergent and exotic diseases will mean that conventional expectations of likely diagnoses by family physicians and primary health care providers will be insufficient. The potential for malaria infection in patients with no history of travel is one such example (63). The increase in extreme weather events such as heatwaves, floods and storms will increase pressure on disaster preparedness and emergency health services and programming (79). Program planning for emergency health provision will need to consider future rather than historical experiences or trends in demand and frequency of health crises (34, 80-82). Increased health surveillance will be required to document baseline health measures and monitor changing health outcomes. This is particularly important in Canada's northern communities where health provision and surveillance have faced significant challenges and where climate impacts will develop earlier and more rapidly than in the South (83, 84).

RESPONSES

The good news is that opportunities for avoidance of, and adaptation to, climate impacts on health are available, feasible, and in many cases of benefit to improved health in Canada more broadly (42). Given the unpredictable nature of many impacts, adaptation, prevention, and preparedness measures that increase overall health system capacity are most sensible and cost-effective – so called 'win win' or 'no regrets' responses (18, 85-89). These include: Increased surveillance, particularly of disease vectors, water quality, and air pollutants; Integration of climate projections into emergency planning and disaster preparedness (79); Improved access to preventive care and primary physician care to promote early detection of new disease emergence or shifting disease incidence; Integration of climate change considerations into education programming for medical students and primary health care workers; Integration of climate projection parameters into urban planning to increase protection against extreme weather events (55, 90-92); Increased monitoring and evaluation of food production systems and water monitoring safety given climate projections (26, 41, 63, 68); Development of heat wave alerts and responses, and mitigation of urban heat islands (41, 52, 53, 91), and; Increased multi-national support for improved health capacity in low and middle income countries.

The risk of health impacts resulting from climate change are not restricted to within our national borders. The impact of climate change elsewhere, particularly in low and middle income nations, will influence the potential for imported infection to Canada. For example, the introduction and outbreak of SARS in Toronto in 2002 resulted in 438 cases, 44 deaths and significant economic losses (93, 94). International travel may have been responsible for promoting the introduction of West Nile virus in North America (95-97). Similarly, a Canadian outbreak of imported malaria in 1995-97 may have been brought to Canada via travelers arriving from the Punjab in India, where a large epidemic had occurred (63, 98-100). More recently, concern regarding the potential spread or proliferation of avian influenza has highlighted the interconnected nature of national health to health conditions around the world. As such, the health impacts of climate change in Canada will be influenced by the health and response capacity of other nations from or to which Canadians, visitors or trade products travel. In this context, adaptation, preparedness and response resources may in some cases be most effectively and efficiently allocated through supporting health capacity in other countries. Increased interest and prioritization of health collaborations in Asia following the SARS outbreak provides a germane example of a developing awareness of such risk priorities.

Despite the magnitude and scope of climate change, the recent global financial crisis has overshadowed concern for, and prioritization of, climate change science, policy, and action. While the implications of economic crisis at the international and national levels are undoubtedly of legitimate priority and concern, placing climate issues on the back-burner is misguided for two reasons. First, while the financial crisis may be acute and possibly prolonged in the short term –years, but not decades – the climate change crisis will last well into the next century and beyond. Investments in health system capacity and surveillance need to be implemented in advance of emerging impacts to avoid and/or mitigate morbidity and mortality. Additionally, observed climate impacts will begin to rapidly accelerate over the next decade. In the absence of genuine and dramatic intervention, climate change impacts have the potential to be severe and acute on a scale greatly exceeding the current financial crisis (3, 4, 6, 7). The lack of action on climate change – including both mitigation of emissions and adaptation to current and future impacts – is generally rationalized based on the costs of interventions. The costs of a no-action approach, however, will be significant. The Stern Review, an independent assessment commissioned in the United Kingdom, estimated that a 5-6 °C warming over the next century could result in losses of up to 20% of global GDP (101); the report estimates the cost of mitigating climate emissions and severe impacts at approximately 1% of global GDP. The health sector, which makes up 10% of Canada's Gross National

Product (GNP) can make a significant contribution to climate change mitigation and adaptation in Canada (102, 103).

It is no longer sufficient to use our past climate experiences to assess health risks and health system requirements. Future health systems and care will need to reflect changing risk conditions; these will differ from what physicians, primary care professionals, and public health professionals are accustomed to. Climate will emerge in the next years and decades as an increasingly important determinant of individual and public health in Canada. Reduced individual and national contributions to greenhouse gas emissions to avoid severe impacts, combined with proactive planning and programming for adaptation will be required.

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FOCUS REVIEW

Food, Global Environmental Change and Health: EcoHealth to the Rescue?

David Waltner-Toews*

Everything is changing, and changing rapidly, except how we think.

What we eat brings issues of health and global environmental change to the table in ways that are urgent, global, and full of scientific uncertainty. Eating is the most intimate relationship we have with the environment, when various parts of plants and animals are integrated into our bodies. Our eating habits link human nutrition (and all the health issues associated with that) and infectious foodborne diseases to agricultural practices, land use, global trade, poverty, economic inequity and climate change.

Official estimates of the incidence of endemic foodborne diseases (as differentiated from outbreaks) from both Canada and the United States show that there were increasing trends from the 1970s to the late 1980s and 1990s. This was the period when Western industrialized countries saw the emergence of new variant Creutzfeldt-Jakob Disease associated with bovine spongiform encephalopathy, serious diseases caused by shiga-toxin-producing E. coli, the pandemic of Salmonella enteritidis and the recognition of listeriosis as a foodborne illness. While one can pinpoint specific causal pathways for each of the diseases, they all reflect more general systemic and cultural changes, including population growth and mobility, a huge shift in agriculture to economies of scale and mass distribution, land use changes including manure production by large livestock enterprises, an expectation of low food costs at the grocery store, relatively low oil costs, better detection methods and a more alert public (1,2).

The increases of the 1980s might be said to have culminated, at least in the public eye, in the 1993 deaths of four children who succumbed to E. coli 0157:H7 infection after eating hamburgers at a fast food restaurant. While this was not the biggest nor most spectacular outbreak of this disease, it coincided with the election of Bill Clinton to the White House, and a serious reworking of food safety procedures in the United States. This was followed by a drop in rates of foodborne infectious diseases for a few years about the turn of the new millennium, and then a settling in to relatively stable rates. The decreases since the turn of the new millennium are probably the result of food industry sobriety and seriousness in the face of more aggressive government regulation, food recalls, litigation, and a worried public. The relative stabilization of rates in the past few years may well reflect a bottom line, the disease costs built into the current structure of the agri-food industry. Indeed, there is now good evidence that global climate change is already increasing occurrences of both foodborne and waterborne diseases in North America, Europe and Australia (3,4).

While the general trends suggest one large story, the particulars of outbreaks in the decade since 1998 are perhaps more telling. There have been repeated outbreaks attributed to Salmonella, E. coli and other enteric pathogens associated with fresh sprouts, almonds, jalapeño peppers, tomatoes, cantaloupe, spinach and lettuce. In other words, infections caused by bacteria normally found in vertebrates are now being transmitted in fresh fruits and vegetables. In the past, one might have attributed such occurrences to cross-contamination in the home, or in a restaurant. The widespread nature of the most recent outbreaks, however, tells a different story. Economies of scale and the fertilizer and water use associated with intensification of production in a few areas, such as California, have led to field conditions that often mimic the insides of warm-blooded animals, allowing bacteria to adapt, evolve and grow. The agri-food industry has kept prices low, in part, by relying on uneducated workers with minimal understanding of food safety

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issues, and few facilities to implement hygienic practices even if they were so inclined. Mass distribution has enabled widespread distribution of the contaminated produce. A warming climate has provided a more congenial environment for the bacteria to proliferate during distribution.

The dilemma is that low food prices in the store enable people on low incomes to have access to more food. This can be a good thing if it improves nutrition and general health status, which is the underlying public health argument in favour of economies of scale and widespread trade. The question nutritionists need to ask is whether the "cheap food" policies are in fact achieving these goals, or if they have become part of the problem (5). There is good evidence that the emergence and global spread of zoonoses – including avian influenza – are related to the same industrial economies of scale that produce more "cheap chicken" (6).

Worldwide, the situation becomes even more complex, and the emergence or increase of foodborne illnesses must be seen in the context of the resurgence of infectious diseases in general (7). Rapid urbanization and population growth have increased demand for meat protein, particularly chicken and pork. The impacts have been seen most dramatically in Southeast Asia, where the response has been a rapid and dramatic shift to economies of scale, but over a much shorter time period and in very different ecological and cultural contexts than in North America and Europe. In North America and Europe, given high investments in technology and health care, one might argue that the negative impacts of salmonellosis, campylobacteriosis, listeriosis and diseases associated with E. coli are the necessary and manageable costs of keeping cheap food on the grocery shelves. Given the collateral environmental and social damage caused by disappearance of small communities, climate change and landscape degradation, many investigators are not willing to concede that argument. In Southeast Asia and elsewhere the case is even less convincing. The increases in duck, poultry and pig production, and the movement of populations and animal production facilities into new landscapes, has led to the emergence of a variety of new infections, including avian influenza and Nipah virus (6).

Physicians who see a whole string of patients with diarrhea in a short time period might be forgiven for thinking that they are in the midst of an outbreak, or an epidemic. For an epidemiologist, the increasing frequency of reported foodborne disease outbreaks raises further questions: are we seeing an outbreak of outbreaks? If so, is there some systemic cause of this?

One of the biggest problems facing those trying to resolve these thorny issues has been a lack of coherent and appropriate research and policy tools. Several authors have attempted to reframe the agriculture-health issues in terms of complex systems analyses (8), but these analyses have to date had little impact on either agricultural policy or health disciplines. The scientific evidence is too fragmented to make anything other than broad inferences, and the policy trade-offs are far from clear (9).

In recent years, there has been an increasing documentation and recognition that the majority of emerging diseases are zoonotic in origin (10,11), and that, at the very least, better communication and coordination among veterinary and medical practitioners is essential. The initial focus on zoonotic diseases reflects the fact that the research methods and management tools are available, the primary obstacle to progress being organization, communication and coordination between human and animal health professionals. Furthermore, there is a unified biomedical tradition to draw on, that stretches from Hippocrates, to Rudolf Virchow and Louis Pasteur, who did not recognize the boundaries between human and animal medicine, and environmental and social change; to William Osler, who was a member of both the McGill medical faculty and the Montreal Veterinary College; Calvin Schwabe, whose 1984 book, Veterinary Medicine and Human Health (12), is a classic in the field; and James Steele, who founded the first veterinary public health unit in the United States.

In this tradition of linking human and animal health, a "One Medicine" or "One Health" movement has emerged, with endorsements from various national and international medical and veterinary associations (see, for instance, www.onehealthinitiative.com and www.oneworldonehealth.org). However, resolution of "one health" problems requires at the very least that one addresses some of the most serious environmental implications of both the problem emergence (land use change leading to loss of the buffering effects of biological diversity and habitat change for disease vectors, changes in the probability of human-agent contact) and the solutions (manure run-off from livestock enterprises designed to improve protein intake by poor people) (13).

There is increasing recognition, then, that the problems of health, ecology and social changes are complex, and embedded in the structures and changes of social-ecological systems (14, 15). This is where "One World, One Health" runs into some serious theoretical and practical challenges. At present, these public assertions appear to be orphaned good ideas, destined to fall victim to a kind of naive sense of global warm feelings. They describe desirable outcomes, but no processes by which one might arrive there, and

hence fall back on inappropriate methodologies. Health scientists have developed excellent methods for developing and testing diagnostics, for evidence-based treatment protocols, and epidemiological designs to tease apart individual risk factors for disease. But these methods were never intended to answer questions such as: How can one best improve human nutrition globally without putting the next generation in jeopardy through environmental and climate change? What are the appropriate policies to foster sustainable human wellbeing?

If the linear causal thinking of laboratory science and conventional epidemiology are inappropriate to answer complex questions in which health is embedded in complex social-ecological dynamics, where can we turn for help?

The answers come from some unlikely sources – the integration of management theories and practices, action research, richer understandings of social and biological ecology and complexity theories. Since the 1970s, when systems theories first became visible outside of the small group of scholars, there have been major innovations of theories of complexity and complex systems, and demonstrated improvements in understanding complex social-ecological phenomena (14,15). With the remarkable exception of studies looking at health issues related to climate change, where complexity is difficult to avoid (16), and some in international agricultural development (17), very little of this integrative, non-traditional scholarship has found its way into the medical and epidemiological literature (18).

Much of the scholarly and practice literature that has taken the challenge of making "One Health" something more than a good idea can be described under the general title of ecosystem approaches to health, or ecohealth for short (15, 19,20). Ecohealth draws on the latest theories of social-ecological complexity and integrates it with publicly-engaged, policy-relevant science. Ecohealth approaches are thus participatory, systems-based approaches to understanding and promoting heath and wellbeing in the context of social and ecological interactions.

Ecohealth may be seen as a way to address, simultaneously, the Millennium Development Goals (http://www.un.org/millenniumgoals/) and the Millennium Ecosystem Assessment (http://www.millenniumassessment.org/en/index.aspx). Indeed, the latter explicitly framed many of its results in terms of complexity and resilience theories. EcoHealth is also the official name of the journal of the International Association for Ecology and Health, and of a major Program Initiative of the International Development Research Centre.

Ecohealth approaches embed a variety of methodological techniques into a coherent, transparent, publicly engaged process of learning, monitoring, and learning again (methodological pluralism). In some ways, it is not so different from what a good clinician does when she integrates a patient history with clinical examination, epidemiological probabilities and laboratory test results to arrive at a reasonable diagnostic conclusion and course of action. Where it differs from clinical medicine is that the boundaries of the patient (Household? Community? Watershed? Globe?), the ownership of the "body", the nature of the complaint (one person's solution is another's problem), the relevant facts in a case, the systemic connections, and the most desirable outcomes are all in dispute.

While these sound like impossible challenges to overcome, they are not. Ecohealth has so far been most successful in situations where the boundaries, stakeholders and desirable outcomes are most apparent. These are often situations where dramatic infectious or toxic outcomes make certain courses of action sufficiently compelling to overcome institutional or individual stakeholder objections. Even in more messy situations, however, where the boundaries are uncertain and there are interactions across multiple scales of policy and practice, various methodologies and guiding questions are being used that are proving to be effective. There is even a sound philosophical basis, emerging from the risk assessment literature, for how the scientific inquiry can (and must) be changed in order to address these questions (15, 21).

This is the cutting edge of public health scholarship and practice. In keeping with its own underlying philosophy and theory, expertise in ecohealth is distributed and networked, rather than residing in particular disciplines or places. There is no critical mass in any one place and, given the dramatically increasing climatic, environmental, and socio-economic instability globally, the focus is on adaptability and the ability to shift and share information, resources and expertise across institutional, disciplinary and national boundaries as rapidly as possible. One of the earliest models for this has been the rapid growth of Promed worldwide (www.promedmail.org), from a small electronic network of interested practitioners to a global network of people working with infectious diseases that detects, tracks and responds quickly to emerging disease signals worldwide.

More recently, and encompassing issues well beyond emerging diseases, we have seen the emergence of Communities of Practice for Ecosystem Approaches to Health (CoPEHs); there are now such networked communities for Latin America and the Caribbean; South and Southeast Asia; Middle East and North

Africa; West and Central Africa; and Canada (see Appendix for websites).

These communities of practice have been started by a variety of scholars and practitioners across a wide range of institutions and disciplines. The CoPEH in South and Southest Asia, which focuses on emerging infectious diseases, was started and is being maintained by Veterinarians without Borders/ Vétérinaires sans Frontières – Canada, with technical assistance from Google.org, and financial aid from the Canadian Food Inspection Agency, the International Development Research Centre, and private donors. Members include individuals and groups from governmental, non-governmental, and trans-national organizations, as well as universities.

The Canadian CoPEH has as its primary objective the promotion and support of research, education, policy and practice in ecosystem approaches to health. Funded by the International Development Research Centre (IDRC), it is directed and administered by a consortium of Canadian universities (University of British Columbia, University of Guelph and Université du Québec à Montréal UQAM). Founding members range from physicians, such as the Head of Family Medicine at UBC, to veterinarians, biologists, philosophers and communications experts.

As part of the educational mandate of this initiative, CoPEH-Canada has created an intensive short course entitled Ecosystem Approaches to Health. In 2008, the course was held in Vancouver at the University of British Columbia. In 2009, it is being held at the University of Guelph; and in 2010 at UQAM. In all cases students are recruited from across Canada and screened by senior members of the CoPEH.

The collapse of the post World War II global economic order, as well as the reorganization of the global climate system, is explainable through an understanding of complex system dynamics. Indeed such collapses and reorganizations are predictable moments in the lives of all systems, although their timing and extent can be modified and altered by human activities – as they have been both economically and climatically. What is of greater interest and urgency, however, is that these same understandings of complexity suggest that we are now at a point of unprecedented opportunity - and a challenge - to reorganize social-ecological relationships in a way that will nurture a sustainable, healthy, human population in a sustainable, healthy planet. Ecohealth offers new and exciting alternatives to understanding and managing changing patterns of foodborne and waterborne diseases in their social, agricultural and economic trading system contexts. This is not a challenge that can be met using more of the same techniques, organizations and lines of inquiry that have brought us to where we are. It requires new ways of thinking, new ways of acquiring and sharing knowledge, and new communities of practice.

APPENDIX:
Communities of Practice for Ecosystem Approaches to Health

- Canada. Focus: Educational development (Canada): www.copeh-canada.org
- Latin America and the Caribbean. Focus: Toxins: http://www.insp.mx/copeh-tlac/eng/inf/index.php
- West and Central Africa. Focus: educational development (French Africa): http://www.copes-aoc.org/
- Middle East and North Africa. Focus: Water Resources Management: http://www.copeh-mena.org/
- South and South East Asia. Focus: Emerging Infectious Diseases: www.copeh-ssea.org. See also www.vwb-vsf.ca.

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CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

Read any good books lately?

T. Jock Murray*

"To study the phenomenon of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all"
Sir William Osler

While emphasizing the place of books and experience with patients in medical education, it was not only medical texts that Osler felt students should read and know. He had a recommended list of bedside books for medical students (Table 1).

In some cases Osler, the most famous of McGill professors, was recommending a body of work rather than a book, and although he was not explicit in what we should take from these writings as future physicians, he clearly felt that these writings contained important teachings and knowledge that would make a student a better physician. Osler himself was a great bibliophile, and his writings are sprinkled with quotations and lessons from an amazingly wide range of classical, fictional and medical literature (1). He donated his great collection of medical and related works to McGill, which formed the basis of the Osler Library in the McIntyre Medical Sciences Building.

A current medical student would understandably regard many of the works on the list as outside their experience and would expect more familiar books on a modern list. If so, what books? What books would students now suggest for a modern list?

Updating Osler's bedside library list has been attempted a number of times (2, 3, 4) and most recently by a group from the American Osler society (5). Dr. Francis Neelon , then President of the AOS, assisted by Dr. Robert Rakel and Dr. Herbert Swick, canvassed members to see if a new list could be developed. It proved a difficult challenge. The Society members were asked how many of Osler's suggestions they had read, and then they were asked to make recommendations for a new list (5). There were 19 responses. Perhaps the nature of Society members, who have a high interest in history, literature and the humanities, and their devotion to Sir William Osler, accounts for the high response to

Osler's bedside table Library for Medical Students

1. Old and New Testament
2. The works of Shakespeare
3. The works of Montaigne
4. Plutarch's *Lives*
5. *Meditations* by Marcus Aurelius
6. *Breakfast Table Series* by Oliver Wendell Holmes
7. *Discourses* of Epictetus
8. *Religio Medici* by Sir Thomas Brown
9. *Don Quixote* by Miguel Cervantes
10. The works of Emerson

Table 1

Some suggestions from members of the American Osler Society (Neelon)

1. Shakespeare
2. Old and New Testament
3. *Don Quixote* by Cervantes
4. *Religio Medici* by Sir Thomas Browne
5. *The Doctor Stories* by William Carlos Williams
6. *William Osler: a Life in Medicine* by Michael Bliss
7. *Life of Johnson* by James Boswell
8. *Man's Search for Meaning* by Victor Frankl
9. Collected Essays by Sir William Osler
10. The Prince by Machiavelli
11. *The Story of Civilization by* Will and Ariel Durant
12. The historical works of Winston Churchill

Table 2

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the reading of Osler's list (Shakespeare 95%; Old and New Testament 84%; Don Quixote 68%; Oliver Wendell Holmes 53%; Religio Medici 42%; Emerson 42%; Marcus Aurelius 37%; Plutarch's Lives 32%; Montaigne 21%; Epictetus 0%).

More interesting is the list of 124 books put forward for a new list by the 19 respondents and some of those with multiple recommendations are appended (Table 2). Some from Osler's original list were among those recommended by more than one person, with top of the list going to Shakespeare, the Old and New Testament, Don Quixote by Cervantes, and Religio Medici by Sir Thomas Browne. Others that were recommended more than once by Society members were various anthologies of poetry, The Doctor Stories by William Carlos Williams, the biography of the great physician, William Osler: a Life in Medicine by Michael Bliss, Life of Johnson by James Boswell, Man's Search for Meaning by Viktor Frankl, Osler's Collected Essays, Machiavelli's The Prince, Will and Ariel Durant's The Story of Civilization, and the historical works of Winston Churchill (Table 2).

Interesting as these books may be, they come from mostly senior and often retired physicians, and although I now am a member of this graying group, I suspect my generation may not be the best to suggest a bedside list for medical students. I wonder if the students themselves couldn't create a relevant list that would resound with their peers.

In my experience, medical students prefer books written by physicians (6). Table 3 has a partial list of physician writers, and there are many other writers who write about medicine.

Students today have more extensive and diverse backgrounds, education and experiences than ever before. It would be enlightening to see a list compiled by medical students. Would there be graphic novels, science fiction or fantasy, pop culture novels? Should the books be inspirational, empowering, educational or just interesting? Would there be podcasts, blogs, magazines? (My own list submitted to the AOS included the Times Literary Supplement and Literary Review which I find highly informative on many subjects and ideas).

Some Physicians writers

Danny Abse	Michael Crichton
Harold Klawans	Walker Percy
John Aiken	Erasmus Darwin
Michael LaCombe	Francois Rabalais
Mary Aikenside	Paul DeKruif
John Locke	Peter Mark Roget
Richard Asher	Sir Arthur Conan Doyle
Saint Luke	Oliver Sacks
Thomas Beddoes	William Drummond
Somerset Maugham	Richard Selzer
Robert Bridges	Macdonald Critchley
Sir Andrew Macphail	Frank Slaughter
Mikhail Bulgakov	Jacques Feron
John MacCrae	Tobias Smollett
Thomas Campion	Sir Samuel Garth
Jonathan Miller	John Stone
Anton Checkov	Oliver Gogarty
Silas Weir Mitchell	Lewis Thomas
Clif Cleaveland	Oliver Goldsmith
Axel Munthe	Abraham Verghese
Robert Coles	Oliver Wendell Holmes
Sir William Osler	William Carlos Williams
Jack Coulehan	Perri Klass
Wilder Penfield	Thomas Young

Table 3

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T. Jock Murray is the former Dean of Dalhousie Medical School and Professor of Medicine (Neurology) and founding director of the Dalhousie Multiple Sclerosis Research Unit. He held the first Chair of Medical Humanities at Dalhousie. He is a past President of the Association of Canadian Medical Colleges and former Chairman of the Canadian Medical Forum. He was the founder of the Dalhousie Society for the History of Medicine, past President of the Canadian Society for the History of Medicine and the President-Elect of the American Osler Society.

Dr. Murray has over 225 medical publications, 9 books, 43 text book chapters, and has held 91 funded research grants. Recent books have been Medicine in Quotations (with Edward Huth), The Quotable Osler (with Mark Silverman and Charles Bryan), and Multiple Sclerosis: The History of a Disease.

CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

A McGill Update of Osler's Bedside Books List

Andrei Liveanu*

Dr Murray ends his article by asking medical students to create a contemporary version of Osler's bedside books for medical students. All current medical students at McGill University were therefore invited to suggest written works that they felt every medical student should read to help them in their development as future physicians. Despite the wide diversity in backgrounds of today's medical students, and despite the somewhat unenthusiastic response rate, some interesting trends can be found. (Table 1)

As Dr Murray predicted, students suggested a number of works written by physicians. Perhaps students gravitate toward these books so that they know what lies ahead for them. *House of God* by Samuel Shem, a novel portraying the demanding life of medical residents was nominated by multiple students. Also popular were works in which one or more of the main characters are physicians: suggestions included *Middlemarch* by George Elliot and *The Cider House Rules* by John Irving.

Works that portrayed physicians in a negative way were particularly popular: students seem to want to be reminded how not to act as physicians. The charlatan physician in Moliere's *Le Malade Imaginaire* or the uncompassionate doctors in Margaret Edson's *Wit* serve as cautionary examples.

The search for ethics and a clear moral code is a second theme that emerges from the survey. Although no two works were suggested twice, examples included *War Against the Weak: Eugenics and America's Campaign to Create a Master Race* by Edwin Black and *Doing Right (A Practical Guide to Ethics for Medical Trainees and Physicians)* by Philip C. Hebert. Interestingly, students seemed concerned not only with ethical issues as they relate directly to their work as doctors-in-training, but also as citizens of the world. Students nominated a number of works that deal with larger issues of their generation, such as *Wealth: Economics for a Crowded Planet* by Jeffrey Sachs and *The Shock Doctrine* by Naomi Klein.

Psychiatry-related books were a third genre popular among student's suggestions. These proposed books included Truman Capote's *In Cold Blood* and Maxime Chattam's *L'Ame du mal*, both literary-style studies of the psychology of serial killers, and *Veronika Decides to Die* by Paolo Coelho, a novel about a teenager who attempts suicide. Through these books, medical students are possibly hoping to prepare themselves to deal with some of the most difficult patients they will encounter.

Among the rest of the suggested books is a mixture of works, ranging from *1984* to the *Harry Potter series* to National Geographic Magazine.

In short, the results of this informal survey were:

- A work about physicians, whether they are portrayed positively or negatively
- A work about ethics, whether medically-related or not
- A work about psychology
- Any of a wide range of light reading

So how does this list compare to Osler's? He too suggested a book about a physician (*Religio Medici*), a book of morals (*the Bible*), and a number of general interest works (Shakespeare, *Don Quixote*). However, while Osler's list contains many works about philosophy, there were none to be found in the contemporary list. And while students suggested many psychiatry/psychology books, none are found on Osler's list.

This informal survey of McGill medicine students is but one more attempt at updating Osler's bedside library list. Yet this list is unique in that it asked current medical students to suggest books for their peers. Not surprisingly, a wide range of works were suggested, but despite the low number of responses, some works were suggested more than once, and many works within a same general theme were suggested. The list therefore points to a degree of agreement among medical students

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as what they ought to be reading beside their medical textbooks. Additionally, this list offers a glimpse into what students think lies ahead for them, and what they think will help them face those challenges.

America by Allan Brandt
Charles Darwin: The Power of Place by Janet Browne
Running with Scissors by Augusten Burroughs
Le Normal et le pathologique by Georges Canguilhem
In Cold Blood by Truman Capote
L'Âme du Mal by Maxime Chattam
A Year in the Merde by Stephen Clarke
Veronika Decides to Die by Pauolo Coelho
Next by Michael Crichton
The Citadel by A.J. Cronin
The Vanishing Man by Jeffrey Deaver
Wit by Margaret Edson (x2)*
Middlemarch by George Eliot (x2)
The Bacchae by Euripides
The Wars by Timothy Findley
T*he Cider House Rules* by John Irving
The Shock Doctrine by Naomi Klein
The Unbearable Lightness of Being by Milan Kundera
Bloodletting and Miraculous Cures by Vincent Lam
Catholic Bioethics by William May
Le malade imaginaire by Moliere
Oh, boy ! by Marie-Aude Murail
Team Medical Dragon by Taro Nogizaka and Akya Nagai
1984 by George Orwell (x2)
The Greatest Benefit to Mankind by Roy Porter
Ishmael by Daniel Quinn
Hope for the children of Kantha Bopha by Beat Richner
Harry Potter series by J.K.Rowling
The Man Who Mistook his Wife for a Hat by Oliver Sachs
House of God by Samuel Shem (x3)^
Say Hello to Black Jack by Sato Shuho
Five Weeks in a Balloon by Jules Verne
Vitals Signs by Barbara Wood
Alcoholics Anonymous: The Big Book
Global Health Watch 2: An Alternative World Health Report
Common Wealth: Economics for a Crowded Planet by Jeffrey Sachs
National Geograhic Magazine
History of Medicine, A Scandoulously Short Introduction by Jacalyn Duffin
Complications: A Surgeon's Notes on an Imperfect Science by Atul Gawande
What Really Matters: Living a Moral Life Amidst Uncertainty and Danger by Arthur Kleinman
Remaking Life and Death: Towards an Anthropology of the Biosciences by Margaret Lock
War Against the Weak: Eugenics and America's Campaign to Create a Master Race by Edwin Black
Cigarette Century: The Rise, Fall, and Deadly Persistence of the Product That Defined
A Country Doctor's Notebook by Mikhail Boulgakov
The God Gene, How Faith is Hardwired into Our Genes by Dean H. Hamer
Doing Right (A Practical Guide to Ethics for Medical Trainees and

Table 1: Results of the survey: A list of all the suggestions put forward by students for a contemporary bedside reading list.
* Work suggested by two different students.
^ Work suggested by three different students.

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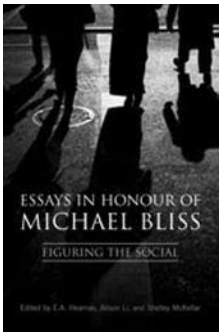
BOOK REVIEW



Book Review by Christine Zadorozny, McGill University,
by Haeman, Li and McKeller, eds

University of Toronto Press,
March 2008,464 pages
ISBN-10: 0802090974
ISBN-13: 978-0802090973
Price: $75.00

Michael Bliss taught and wrote upon a few basic historical themes – medicine, business, and politics – in analyses that were alternatively framed as large-scale events or as individual life stories. In his own academic career, he moved from one special subject to another, showing a certain defiance of narrow academic boundaries.

Thus reads the introduction to Figuring the Social, a collection of essays published by the University of Toronto Press in honour of Canadian historian Michael Bliss. This anthology, edited by E.A. Heaman, Alison Li and Shelley McKellar, consists of dissertations written by students and colleagues of Bliss, who has produced notable works such as The Discovery of Insulin, Plague: A Story of Smallpox in Montreal and a biography of Sir William Osler, entitled William Osler: A Life in Medicine. In addition to his work in the area of medical history in Canada, Bliss has also written extensively about the business and political history of this country. It is, perhaps, due to the wide scope of Bliss's work that the essays presented in this anthology resist categorization under any particular theme. Rather, they vary quite widely in both style and subject matter, from one author's reflection on his professional relationship with Bliss to another's examination of the relationship between Charles Gordon (also known as novelist "Ralph Conner") and Gordon's son, King. While Bliss' dexterity with a wide variety of subjects is to be lauded, however, the attempt of the editors to mirror this diversity results in a compilation of essays that can seem out of place next to one another – a little more thematic cohesion would have given the collection more strength. That being said, there are some thought-provoking essays in this book that are well worth a read by anyone who is interested in Bliss' work, in his philosophies, or in the history of medicine in Canada.

The first essay in the collection is an autobiographical piece by Bliss himself. In it, he describes the course that his career prospects and world-view have taken since his childhood. The son of a physician, Bliss reports that "from the time I could talk I would automatically say that I wanted to grow up to be a doctor." However, he changed his mind at the age of fourteen:

> *... there was a Sunday afternoon when Dad's and my Scrabble game was interrupted by the appearance at the office door of a policeman with a drunk in tow, the drunk having been in a fight and suffering a badly slashed face. Dad had to sew him up, suturing both inside and outside the cheek, and invited me to watch what would be a demonstration of his surgical skill [...] with blood and alcohol fumes everywhere, reflecting on my own complete disinterest in and lack of manual skills, I decided that this was not what I wanted to do in life. And that was the end of my ambition to be a doctor.*

Bliss parallels this moment of revelation with a similar decision made by famous physician, teacher and essayist Sir William Osler. Bliss reports that Osler, the son of a Minister, also forsook his father's trade for another – with the belief that "man's redemption of man" could mean more on earth than the type of redemption that a Minister offered to his parishioners. Bliss situates himself firmly within this tradition, saying that "in looking at the history of medicine we are studying, revealing, and, when it is appropriate, celebrating human achievement aimed at the redemption and salvation of humankind. This is the great satisfaction I find in doing medical history." An excellent essay by Allison Li on the transformation of endocrinology brought on by insulin further highlights Bliss' fascination with the revivifying possibilities afforded by medicine, quoting him as saying that the effects of insulin were the "closest approach to the resurrection of the body that our secular society can achieve."

Figuring the Social contains essays on the subject of Michael Bliss' career path and influence as well as dissertations on subjects in politics, business, religion, family, health policy and the practice of medicine in Canada. This latter section contains historical pieces on subjects such as the response of the Canadian

government to the thalidomide tragedy, the origins of the Connaught Medical Research Laboratories in Toronto and their influence on Canadian Public Health Policy, and an essay entitled "Comfort, Security, Dignity: Home Care for Canada's Aging Veterans, 1977-2004," which provides an overview on Canada's policies on veteran health care during this time period. Other articles on the subject of health include a history of lobotomy in Ontario, a discussion of medical biography and autobiography as a genre, and an account of the pursuit to develop a mechanical heart undertaken by William Kolff, inventor of the artificial kidney.

This anthology might have been stronger if it had focused on one particular aspect of Bliss' work. For instance, Bliss' discussion of medical history in his essay is well paired with the historical accounts found in the later chapters on health in Canada. If, as Bliss describes, medicine is an attempt at "man's redemption of man" on earth, which is more successful: the practice of medicine itself or its figuration and chronicling in history? Medicine can prolong the life of individuals – history prolongs our memory of them and can figure them in new ways, beyond what is possible in a lifetime. According to Bliss,

> *There is the immensely frustrating fact that health care offers only temporary salvation. It buys time, but the time always runs out – even for those virtually resurrected children who outlived every one of the discoverers of insulin. They're all dead now. We can assault morbidity, we can postpone mortality, but we can't change the absolute mortality rate, which is permanently stuck at 100 per cent. Which means, of course, that the deal Osler offers us, of salvation through physical health and health care – he called it a "ministry of health" – is hugely unsatisfactory compared to what Osler's father peddled, which was life everlasting.*

The strength of this anthology lies in its exploration of medicine's pursuit to preserve life. This is a goal that is both absolutely worth striving for and, as is illustrated by the dramatic outcomes of the discovery of insulin, is one that medicine can definitely achieve. And yet, as Bliss points out, it is eventually bound to fail as human life cannot be prolonged indefinitely. This is where the historian steps in to record and present these achievements to the generation to come, endowing them with a "life everlasting" of their own.

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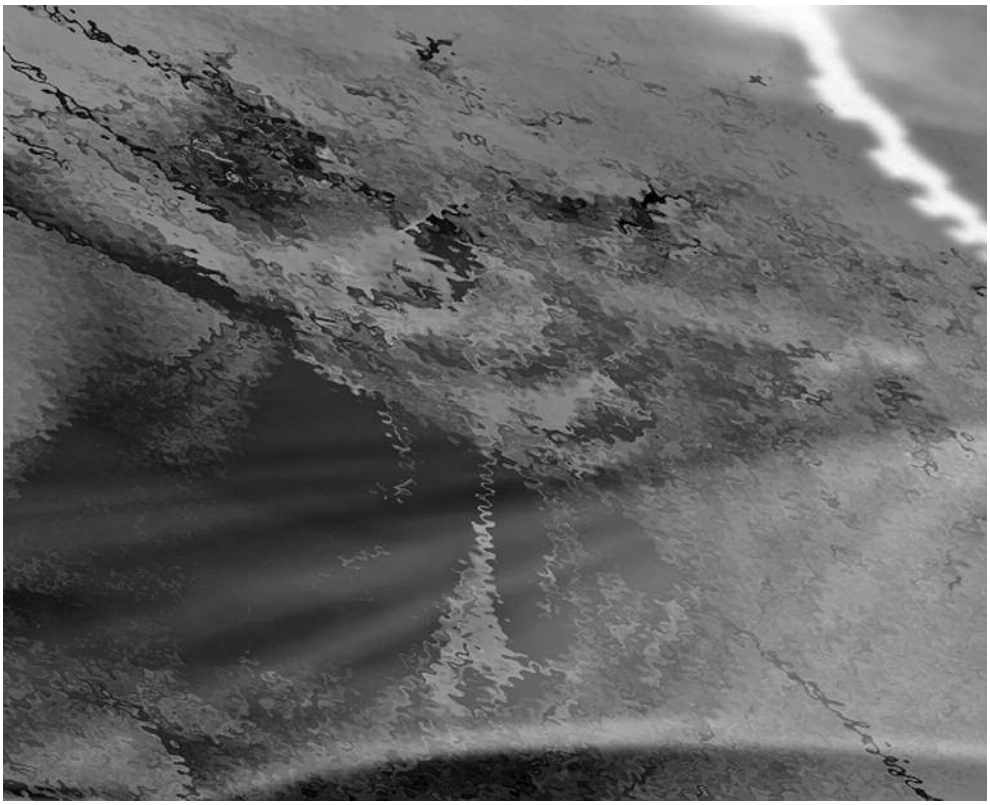

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