Diabetes in Aboriginal populations

I am concerned that Philip Hall's description of the health status of aboriginal people in North America before their first contact with Europeans[1] might, albeit unintentionally, reinforce the stereotype of a robust, essentially disease-free "noble savage" practising good nutrition supplemented with plenty of fresh air and exercise. The only infectious disease predating European contact that Hall alludes to is syphillis; he lists tuberculosis among the post-contact diseases. In fact, *M. tuberculosis* acid-fast bacilli have apparently been found in the mummified remains of a young Peruvian boy whose death is estimated to have occurred approximately 800 years before the arrival of Columbus.[2] Tubercular-type bony lesions have also been documented in skeletal remains discovered in a pre-contact ossuary in southern Ontario.[2] Moreover, the traditional food supply was neither pristine nor ideal. Examination of coprolites provides evidence of meat-borne parasitic infections that could at worst infect the lungs and central nervous system or at best the alimentary tract. The maize diet produced circular dental caries similar to lesions found today in children from developing countries, a consequence of malnutrition caused by chronic diarrhea.[2]

I agree that the prevalence of diabetes is influenced by both geographic and genetic variables, but I would add socioeconomic variables to the list. A recent study of prescription drug utilization among aboriginal people in Canada shows higher rates of use of certain analgesic and anxiolytic drugs than among the general Canadian population; these are not unlike the differences in rates of diabetes between the 2 groups.[3] However, drug utilization rates among aboriginal people are strikingly similar to the rates within the portion of the nonaboriginal population whose socioeconomic characteristics are similar to those of the aboriginal population. These characteristics include poverty, unemployment, lower education and substandard housing. Furthermore, although aboriginal Canadians with diabetes may die from the disease at a rate 2 to 4 times higher than that among other Canadians with diabetes, overall mortality rates among aboriginal Canadians are also significantly higher. We must consider factors beyond genetics and lifestyle when we explain differences in health status.

John F. Anderson
Community Health Programs
BC Ministry of Health
Victoria, BC

References

1. Hall PF. Ironies most bittersweet. *CMAJ* 1999; 160(9):1315-6.
2. Waldram JB, Herring DA, Young TK. *Aboriginal health in Canada: historical cultural and epidemiological perspectives.* Toronto: University of Toronto Press; 1995.
3. Anderson JF, McEwan KL. Utilization of common analgesic and anxiolytic medications by registered First Nations residents of western Canada. *Subst Use Misuse* 2000;35(4):169-84.

[The author responds:]

I agree with most of John Anderson's assertions, especially the last sentence, and if my writing reinforced anyone's stereotypes that was unintended. My purpose was to provide a partial explanation of diabetes as a novel epidemic in North American aboriginal groups and to argue that the epidemic of type 2 diabetes world wide has its main roots in genetic predisposition, dietary change, obesity and sedentarism.[1,2] I am sure that *CMAJ* readers would realize that the disease is also correlated intimately with socioeconomic variables.

Anderson may be correct that I should not have included tuberculosis in my list of infections unknown to "New World" tribes before European contact; in addition to the remains he mentioned, tubercular DNA was extracted from various human bones from Chiribaya Alta in southern coastal Peru. However, some researchers still consider that the presence of tuberculosis in the Americas before Columbus is unproven.[3]

I chose to refer to syphilis partly because, aside from tobacco, it was the only New World export that had a devastating effect in Europe. There are as many bittersweet ironies about the chronicles of tuberculosis and syphilis as there are about diabetes. The 2 infections have been linked, and confused, for centuries. In 1527 Jacques de Béthencourt provided a remarkably accurate description of the pox, stressing its polymorphic character, that it could cause osseous deformity and cavitation, and that it shared some characteristics of consumption. The answer to one of *M. tuberculosis*' enduring mysteries — how and when it migrated globally[4] — may remain forever obscured by the organism's antiquity. It is curious that syphilis and tuberculosis penetrated European populations thoroughly, whereas native North Americans – judging from history and the examination of human remains — were more resistant to both infections. While 1 in 4 16th-century Europeans were dying from tuberculosis, their Mesoamerican contemporaries were dying in large numbers from the more direct results of contact with the conquistadores. Although the Peruvian boy mentioned by Dr. Anderson took his last tubercular breath around 700 AD, his culture expired when Francisco Pizarro's troops executed Atahualpa, the last Incan Emperor, in 1532.

There is stong evidence that syphilis was brought to Europe on Columbus' caravels. Contemporary European authors agreed that the disease was new. For example, Gonzalo Fernandez de Oviedo y Valdes was at court when Hernando and Isabel received Columbus after his first voyage. After interviewing the sailors and their captives he considered it to be "certain that this malady — the bubas — comes from the Indes, where it is very common amongst the Indians."[5]

When Columbus died, crippled by gout and arthritis, in 1506, it is unlikely that he had any idea of the consequences of his ventures. Nonetheless, the world had been "changed, uprooted

and catapulted out of life-patterns that had endured for thousands of years."[6]

Philip F. Hall
Department of Obstetrics and Gynaecology
University of Manitoba
Winnipeg, Man.

References

1. Kopelman PG, Hitman GA. Exploding type II. *Lancet* 1998;352(4 suppl):5.
2. Xiong W, Gray JD. The roles of receptor abnormalities in the pathogenesis and chronic complications of type 2 diabetes mellitus. *Clin Invest Med* 1999;22(3):85-106.
3. Diamond J. *Guns, germs and steel: the fates of human societies*. New York: W.W. Norton; 1999. p. 357.
4. Small PM. Towards an understanding of the global migration of tuberculosis [editorial]. *J Infect Dis* 1995;171:1593-4.
5. Fernandez de Ovieda y Valdes G. *Oviedo de la natural historia de las Indias* [Summary account of the natural history of the Indies]. Toledo; 1526.
6. Bradley M. *The Columbus conspiracy*. Toronto: Hounslow Press; 1991.

A worthy Web site

I recently underwent a set of screening, then diagnostic, mammograms, followed by 2 ultrasounds and a biopsy. I found trying to gather reliable and comprehensive information about breast health issues by phone, in person and online to be an exercise in sleuthing and perseverance — until I came across the *CMAJ* Web site (www.cma.ca/cmaj), which is offered at no subscription cost. It provided a clear, concise and complete guide to all of the questions to which I needed answers in order to be informed at each stage of the screening and diagnosis process.

Thank you for providing an informative and helpful online resource to both health care practitioners and lay people.

E. Jill Watson
Toronto, Ont.

Anticoagulant prophylaxis against stroke

Jaime Caro and colleagues are to be congratulated for their study confirming the beneficial effect of anticoagulants to prevent stroke in atrial fibrillation.[1] In the same issue Stuart Connolly asks why so many eligible patients are not receiving anticoagulant therapy.[2] I would suggest the following possible reasons.

First, patients may be reluctant to go to a testing laboratory on a regular basis. They may also be concerned about the restrictions the use of blood thinners may impose on their lifestyle.

Second, there is the issue of informed consent. Using the results of the study by Caro and colleagues, a diligent physician might explain to a patient that the risk of stroke in individuals taking warfarin is 2.3 per 100 person-years as opposed to 6.7 per 100 person-years in the no-treatment group and that the hazard rate from bleeding is 3.4 per 100 person-years in the warfarin group versus 1.9 per 100 person-years in the no-treatment group. The patient might assume that taking warfarin would mean going from the frying pan into the fire.

The third reason is physician reluctance. Connolly makes no mention of the increased workload anticoagulant therapy places on the treating physician and his or her staff. Whenever a patient goes for a blood test, the international normalized ratio (INR) results are typically phoned into the physician's office. The physician must then modify the dose as required and notify the patient of any changes. This requires several phone calls and can be a major source of anxiety (and possible medicolegal liability) when, for whatever reason, the doctor's office is unable to reach the patient to make the required medication changes. Admittedly, in BC physicians do get paid the princely sum of $2.73 for providing this service.

John Sehmer
Family physician
Vancouver, BC

References

1. Caro JJ, Flegel KM, Orejuela ME, Kelley HE, Speckman JL, Migliaccio-Walle K. Anticoagulant prophylaxis against stroke in atrial fibrillation: effectiveness in actual practice. *CMAJ* 1999;161(5):493-7.
2. Connolly SJ. Preventing stroke in atrial fibrillation: Why are so many eligible patients not receiving anticoagulant therapy? [editorial] *CMAJ* 1999;161(5):533-4.

Reference-based pricing

We found the articles by Lutchmie Narine and colleagues[1] and Chantal Bourgault and associates[2] to be of particular interest, as we have been involved in the development of the Reference Drug Program in BC from its inception. The program has received both criticism and accolades since it was launched in the fall of 1995. Criticism has come primarily from the pharmaceutical industry, as any savings that governments achieve from the application of the policy are also reduced profits for the drug companies. Indeed, it has been stated that one gauge of any policy's effectiveness is the vigour of the industry response.[3] Accolades have come from those who recognize the importance of a sustainable drug program for the long term.

Narine and colleagues[1] attempt to draw correlations between the reference pricing policies in Europe and those in BC. Although there may be some similarities, there are significant differences. The primary focus of the policy in BC is the baseline prescribing habits of physicians. The policy is designed to ensure that the most cost-effective agent within a drug class is used initially. If there are particular patient circumstances that would justify the use of a more costly agent, such as an adverse reaction or lack of therapeutic effect, the alternative agent is funded fully. In addition, the Reference Drug Program in BC does not target generic equivalents as stated in the article, but rather it targets competing drugs in a class.

Bourgault and associates[2] review the utilization of a select group of angiotensin-converting-enzyme (ACE) inhibitors, as well as hospital admissions and physician visits. Although the authors speculate that there are therapeutic differences among the ACE inhibitors, they present little evidence to support this assertion.

We agree with the critical comments by editorialists Paul Grootendorst and Anne Holbrook.[4] There are many plausible explanations for the differences in health services utilization rates ob-

served. In addition to it being the ACE inhibitor of choice in hypertension at the time, captopril was likely available on all the hospital formularies in the province at the time. As it is unlikely that many hospitals included lisinopril on their formularies in the early 1990s, it is entirely possible that patients in hospital were preferentially prescribed captopril simply because of its availability and therapeutic efficacy.

Bob Nakagawa
Reference Drug Program Expert Advisory Committee
BC Ministry of Health
Port Moody, BC
Rick Hudson
Clinical Support Unit
BC Ministry of Health
Victoria, BC

References

1. Narine L, Senathirajah M, Smith T. Evaluating reference-based pricing: initial findings and prospects. *CMAJ* 1999;161(3):286-8.
2. Bourgault C, Elstein E, Le Lorier J, Suissa S. Reference-based pricing of prescription drugs: exploring the equivalence of angiotensin-converting-enzyme inhibitors. *CMAJ* 1999; 161(3):255-60.
3. National Forum on Health. *Canada health action: building on the legacy*. Ottawa: The Forum; 1997.
4. Grootendorst P, Holbrook A. Evaluating the impact of reference-based pricing [editorial]. *CMAJ*1999;161(3):273-4.

In a study of reference-based pricing, Chantal Bourgault and colleagues[1] challenge the therapeutic equivalence of 3 ACE inhibitors on the grounds that patients with hypertension whose treatment was started with captopril had more subsequent hospital admissions and ambulatory medical visits than those who were initially prescribed enalapril or lisinopril.

First, it is unclear why they used an intention-to-treat analysis. What they needed to determine was whether the medication used was the cause of these outcomes. In a recent Canadian study[2] by 3 months 13% of patients with hypertension who were initially prescribed an ACE inhibitor did not persist, and by 4.5 years only 53% were still taking that medication.

Second, before wading into a database analysis to look for correlations, there should surely have been a more precise statement of a clinically plausible hypothesis than, I wonder if all 3 drugs are associated with the same admission rate? These were patients who were starting treatment for uncomplicated hypertension, a condition that is unlikely of itself to be the cause of hospital admissions.

Was the hypothesis then that captopril was less effective in controlling blood pressure, and that this caused a higher incidence of heart disease and stroke in the subsequent 4 years? There is ample evidence that blood pressure control with these 3 agents is fairly comparable, and even if blood pressure was less well controlled, the resultant increase in heart disease and stroke would be unlikely to appear so rapidly.

Or was the hypothesis that with captopril there would be more side effects or drug interactions of sufficient severity to warrant hospital admission? These hospital discharge diagnoses, which were ascertained but not reported, would surely tell us the reason for hospital admission and would suggest the way in which captopril was (or was not) the cause of increased admission rates.

Numerous possible reasons for this result, other than the absence of therapeutic equivalence, are cited in this paper and in an accompanying editorial.[3] The most likely explanation is that the patients initially prescribed captopril were more sick before therapy started than the patients prescribed the other drugs, as evidenced by higher drug use and higher admission rates. Surely one can never say that one has corrected for this, but only that one has tried to correct for this.

I think we should conclude that this is a provocative study that merits clarification, but the conclusion that the result "suggests that ACE inhibitors may not be therapeutically equivalent" is premature.

Maurice McGregor
McGill University Health Centre
Montreal, Quebec

References

1. Bourgault C, Elstein E, LeLorier J, Suissa S. Reference-based pricing of prescription drugs: exploring the equivalence of angiotensin-converting-enzyme inhibitors. *CMAJ* 1999; 161(3):255-60.
2. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD. Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual practice data. *CMAJ* 1999; 160(1):41-6.
3. Grootendorst P, Holbrook A. Evaluating the impact of reference-based pricing [editorial]. *CMAJ* 1999;161(3):273-4.

[The authors respond:]

One of the ways to move beyond partisan discussion about the BC Reference Drug Program is to begin looking at the objective evidence of the program's effectiveness, as we did in our article.[1] Although we are pleased that our study has drawn interest and comment from those involved in the development of the program, it is unfortunate that the comments were directed at clarifying perceived misstatements that in our view are not present in the article.

Bob Nakagawa and Rick Hudson question our comparison of the BC reference pricing policy with those in Europe, citing differences between the policies. A careful reading of our article will reveal that we are aware of these differences and so did not attempt to make any correlations beyond indicating that jurisdictions in Europe experimented with this form of policy before BC and reporting that as in Europe the initial effect of the BC program has been a decline in annual drug expenditures. We devoted a paragraph to listing how the BC program differed from others, and in particular we indicated the existence of "an option for special authority approval, which provides full coverage for a more expensive drug if the prescribing physician can justify its use."

Nakagawa and Hudson indicate that we stated that the BC program targets generic equivalents. At no point did we make such a statement. If this were so, our analysis and presentation of data would have highlighted generic equivalents. We did indicate in the article that reference-based pricing may be most applicable to a limited segment of the pharmaceutical market that includes therapeutic categories containing generic equivalents. This statement was

made as part of a general discussion about why reference-based pricing policies may not substantially slow the growth of pharmaceutical expenditures in the long term and did not refer to the BC program specifically.

Lutchmie Narine
Mahil Senathirajah
Tina Smith
Department of Health Administration
University of Toronto
Toronto, Ont.

Reference

1. Narine L, Senathirajah M, Smith T. Evaluating reference-based pricing: initial findings and prospects. *CMAJ* 1999;161(3):286-8.

Bob Nakagawa and Rick Hudson suggest that captopril was the ACE inhibitor of choice in hypertension at the time of our study and that patients in hospitals might have been preferentially prescribed captopril. Our data, however, show that among first-time users of ACE inhibitors, the use of captopril was considerably lower than that of the other 2 agents; this does not indicate preferential use of captopril initially. Moreover, our study included only prescriptions dispensed on an outpatient basis, and availability of the drug on the hospital formularies should not have direct relevance to our study. Thus, we disagree with the claim that we present "little evidence" of the presence of therapeutic differences among ACE inhibitors on that basis.

Maurice McGregor contends that our conclusions are premature. He refers to a study by Caro and colleagues[1] that showed very low rates of persistence with ACE inhibitors in a similar cohort. We agree entirely that one should take such changes in drug use into account when trying to infer causality between drug use and subsequent use of health services, which our study did not. Our intent-to-treat analysis was a first step in using population-level data to assess whether agents belonging to the same therapeutic class differ in respects other than simply their chemical structures, such as the way they are prescribed to different patients and their impact on health services utilization. Additional studies accounting for complex patterns of drug use would be welcome.

Reference-based pricing policies aim to ensure that the more cost-effective medication is used. Although we are advocates of this approach, we believe that such policies should be carefully evaluated, not only in terms of health-related spending but also in terms of population health. McGregor's statement that "this is a provocative study that merits clarification" is certainly true. Indeed, our study had several methodological limitations, as Paul Grootendorst and Anne Holbrook correctly pointed out in an accompanying editorial,[2] and there may be other plausible explanations for the observed differences. However, population-based studies are essential in evaluating whether policies aimed at reducing costs may not in fact increase long-term costs and, more important, negatively affect public health.

Chantal Bourgault
Samy Suissa
Department of Epidemiology and Biostatistics
McGill University
Montreal, Que.

References

1. Caro J, Speckman JL, Salas M, Raggio G, Jackson JD. Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual practice data. *CMAJ* 1999; 160(1):41-6.
2. Grootendorst P, Holbrook A. Evaluating the impact of reference-based pricing [editorial]. *CMAJ* 1999;161(3):273-4.

Much ado about Furbies

The research letter by Kok-Swang Tan and Irwin Hinberg regarding the Furby toy[1] raises questions. Was more than 1 Furby tested? There may be variance among Furbies. How did they obtain the Furby? When I tried to get one at Christmas time in 1998, they were virtually impossible to obtain. Did they use expensive AAA batteries, or cheaper ones that might reduce the electric and magnetic fields generated by the Furby? Finally, they state that the electric and magnetic field strengths generated by the Furby were about "70 times weaker" than those from a digital telephone. One time weaker would obviously mean no electromagnetic waves whatsoever, but it is hard to picture something that is 70 times weaker. Does this mean 1/70th, or 70% less? Or do the Furbies actually absorb electromagnetic waves, being in a negative mode?

Walter Ewing
Medical consultant
Ontario Ministry of Health and Long-Term Care
Toronto, Ont.

Reference

1. Tan K-S, Hinberg I. Furby does not interfere with medical devices. *CMAJ* 1999;161(8):971.

[One of the authors responds:]

We tested 2 Furbies. Neither caused any effect on medical devices. We had no difficulties in obtaining the Furbies. We obtained one from the Canadian distributor in Montreal and the other from a friend. Many colleagues had offered to lend us their Furbies for testing. We used 4 Energizer alkaline batteries. The voltage of each battery was checked after each test to ensure that it had not fallen below 1.50 V DC (about 94% of the initial voltage). As we pointed out in our paper the electric and magnetic field strengths generated by the Furby were weak — not zero. The term "70 times weaker" means 1/70th the strength.

Kok-Swang Tan
Research scientist
Health Canada
Ottawa, Ont.

Old ways of treating TB may hold new appeal

As a physician who was involved in treating tuberculosis before the introduction of chemotherapeutic drugs, I found the article by Earl Hershfield

on the treatment of tuberculosis most enlightening.[1] I left the tuberculosis field when it seemed as if these drugs were going to revolutionize therapy, as they have to a great extent.

However, it seems that now we are facing an onslaught by drug-resistant bacilli. It may well be time for phthisiologists to look at the older treatments, such as collapse therapy by artificial pneumothorax and pneumoperitoneum, thoracoplasty, phrenic nerve crush and the old standby, prolonged bed rest. Perhaps some of us older physicians may be called on to help, while we are still around and remember how these treatments were carried out.

Frank Jackson
Diagnostic radiologist
Edmonton, Alta.

Reference

1. Hershfield E. Tuberculosis: 9. Treatment. *CMAJ* 1999;161(4):405-11.

A false-positive tuberculin test result

The tuberculin test can be helpful in the diagnosis of *Mycobacterium tuberculosis* infection. A recent *CMAJ* article mentions that false-positive test results can occur in those who have received BCG (bacille Calmette-Guérin) vaccination in childhood[1] but that positive reactions usually wane over time. No mention is made of the effect on the tuberculin test of intravesicular BCG therapy.

Patients with a positive tuberculin test reaction are usually asked if they have a history of BCG vaccination; however, most physicians do not ask their elderly patients if they have a history of intravesicular BCG therapy, which is commonly used for bladder cancer.[2] The following case illustrates how careful review of a patient's history and medical records confirmed a false-positive reaction.

A 74-year-old man presented with a 9-kg weight loss. A chest x-ray film revealed fibrotic changes in the left lower lobe. A Mantoux test was strongly positive with induration of 18 mm at 48 hours. The patient denied constitutional symptoms of fever, chills or night sweats. He had a mild dry cough. He denied hemoptysis. He had been smoking for 60 years and had a history of emphysema and throat and bladder cancer. There was no history of exposure to tuberculosis, and he did not recall having a BCG vaccination in childhood. He had a negative tuberculin skin test in 1995. Chest CT showed old granulomatous changes and emphysema. The possibility of active tuberculosis was entertained. Findings on the chest x-ray film were unchanged from 1991. Urine and sputum cultures for acid-fast bacilli were negative. Isoniazid prophylaxis was considered in view of induration of 15 mm or greater and recent conversion.

The patient did not know what treatment he had received for bladder cancer other than that it was some form of "chemotherapy," but hospital records confirmed that he received intravesicular BCG immunotherapy in 1996. The recent tubercular conversion was concluded to be false positive and isoniazid prophylaxis was avoided.

Among patients given intravesicular BCG treatment for superficial bladder cancer, up to 65% may have a positive tuberculin skin test reaction.[2] For patients with a positive reaction who have a history of bladder cancer, physicians should investigate whether they have had intravesicular BCG therapy before they commit to isoniazid prophylaxis.

Malvinder S. Parmar
Nephrologist
Timmins, Ont.

References

1. Menzies D, Tannenbaum TN, FitzGerald JM. Tuberculosis: 10. Prevention. *CMAJ* 1999; 161(6):717-24.
2. Lamm DL. Bacillus Calmette-Guerin immunotherapy for bladder cancer. *J Urol* 1985; 134(1):40-7.

Corrections

A recent article by Charlotte Gray[1] attributed information on the shortage of anesthetists in Canada to the Canadian Institute of Health Information. The information was correct, but it should have been attributed to the Canadian Anesthesiologists' Society.

Reference

1. Gray C. How bad is the brain drain? *CMAJ* 1999;161(8):1028-9.

The author byline for the specialty spotlight on xenotransplantation in the Nov. 16 issue[1] should have read "Lindsay E. Nicolle, MD."

Reference

1. Nicolle LE. Xenotransplantation: An animal future? *CMAJ* 1999;161(10):1291.

A copyediting error was made in a recent article by Paula Rochon and colleagues.[1] The first sentence in the Interpretation section (page 1406) should have read: "We found that almost half of all patients in Ontario aged 66 or more who survived an MI did not receive β-blocker therapy despite its proven secondary prevention benefit."

Reference

1. Rochon PA, Anderson GM, Tu JV, Clark JP, Gurwitz JH, Szalai JP, Lau P. Use of β-blocker therapy in older patients after acute myocardial infarction in Ontario. *CMAJ* 1999;161(11):1403-8.

The number of articles retrieved in a MEDLINE search using the search terms peppermint oil and irritable bowel was reported incorrectly in recent letters to the editor.[1,2] MEDLINE lists 13 articles on peppermint oil and irritable bowel.

References

1. Lépine P. Reaching a consensus on irritable bowel syndrome. *CMAJ* 1999;161(10):1237.
2. Paterson WG, Thompson WG, Vanner SJ, Faloon TR, Rosser WW, Birtwhistle RW, et al. Reaching a consensus on irritable bowel syndrome [reply]. *CMAJ* 1999;161(10):1237.

The author of the final letter to the editor on the CMA Charter for Physicians in the Nov. 30 issue[1] is Derryck H. Smith of Vancouver, BC.

Reference

1. Smith DH. Cheers and jeers for the Charter for Physicians. *CMAJ* 1999;161(11):1396.