St. John's Wort Warning

Reduces effectiveness of cancer drug

In a study published in the November 2004 issue of *Pharmacotherapy* and the August 15, 2004 issue of *Blood,* University at Buffalo researchers report that the herbal supplement St. John's Wort undermines the effectiveness of Gleevec,® a cancer drug that in recent years has revolutionized the treatment of chronic leukemia.

By Mary Cochrane

"We found that St. John's Wort may significantly reduce the effect of Gleevec by lowering blood levels to the point where patients may fail therapy if they take both together," says Patrick F. Smith, PharmD, assistant professor in the School of Pharmacy and Pharmaceutical Sciences, who was the study's principal investigator and lead author.

"Patients may not view alternative products as 'medications,' and thus they frequently go unreported to the patient's physician or pharmacist," he adds. "In many cases, patients may not need these herbal products and don't know that there may be serious drug interactions. There may also be certain prescription or non-prescription alternatives to a particular product that may be safer and could be used at the recommendation of the patients health-care providers."

The UB study is timely because recent surveys show that the use of alternative supplements such as St. John's Wort has increased tremendously over the past decade, particularly among cancer patients. Adding to this data, Smith and his colleagues report that approximately one-third to one-half of all cancer patients utilize some type of alternative supplement, such as vitamins and herbal products.

Gleevec (imatinib mesylate, Novartis), which is taken in pill form, was the first drug to specifically target cancer cells without affecting normal cells, making it relatively non-toxic, unlike traditional chemotherapy drugs.

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"Hence, it is the first drug that turns cancer into a chronic disease that is treatable with a tablet, similar to high blood pressure or diabetes," says Smith.

Due to its effectiveness, Gleevec received expedited approval from the U.S. Food and Drug Administration for the treatment of chronic myeloid leukemia and has rapidly become a cornerstone of cancer treatment, according to Smith.

Taking St. John's Wort, commonly used for mood elevation in cancer patients, along with Gleevec "will unnecessarily put patients at risk for failure and resistance during treatment because it increases a patient's metabolism of the medication, which results in the drug being eliminated more quickly than normal from the body," explains Smith. "This in turn lowers the blood levels, or reduces the patient's exposure to the medication, decreasing its effectiveness.

"If blood levels are too low, the other thing that can happen is that the leukemia cells can become resistant to Gleevec, rendering it completely ineffective, even if the dose is increased," he adds.

Similar results have been described in drug interaction studies of St. John's Wort with medications for AIDS, notes Smith, who believes cancer patients should avoid herbal supplements in general during treatment.

"We need to do a better job of educating physicians as well as the public regarding the hazards of taking these herbal products, which are unregulated by the FDA," he concludes.

"It's imperative that patients know that herbals are not regulated and that they may be very dangerous when combined with certain drugs. Patients should always check with their physician or pharmacist before taking any herbal or over-the-counter product. Their lives literally may depend on it."

The clinical studies performed by Smith and his colleagues were conducted in the Buffalo VA Medical Center's Clinical Research Center. Co-authors of the study in UB's School of Pharmacy and Pharmaceutical Sciences include Julie Bullock, PharmD, Brent Booker, PharmD, Curtis Haas, PharmD, Charles Berenson, MD, and William Jusko, PhD. BP

Trafficking in Asthma

A recent study by University at Buffalo researchers shows that residents of neighborhoods located within one-third of a mile of the Peace Bridge in Buffalo—the busiest U.S.-Canada border crossing in the Northeastern U.S.—are four times more likely to suffer from asthma than those who live more than 1.25 miles away.

The study, published in the July 2004 issue of the *American Journal of Public Health,* is the first to document how living near the Peace Bridge affects residents.

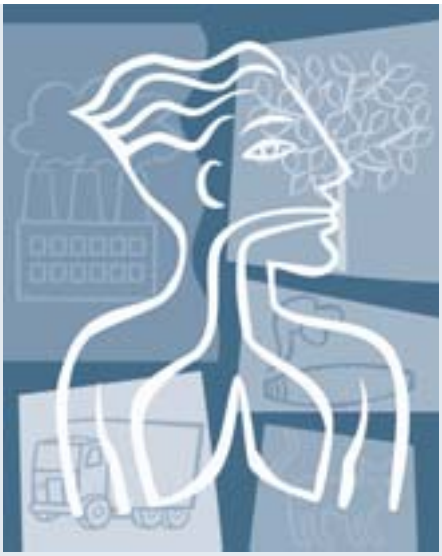
By Ellen Goldbaum

The researchers say that these findings, which corroborate research from other groups as well as their own, underscore the fact that public health should be considered when transportation policies are made.

"Transportation decisions need to include health considerations," says the paper's co-author, Jamson Lwebuga-Mukasa, MD, associate professor of medicine in the School of Medicine and Biomedical Sciences and director of UB's Center for Asthma and Environmental Exposure. "Our findings are especially relevant since the volume of commercial traffic at this border crossing point will quadruple by the year 2020," he adds, referring to the plans to expand the Peace Bridge Complex to accommodate more commercial traffic.

Lwebuga-Mukasa notes that while public debate in the community over how to expand the bridge has focused on the displacement of neighborhoods and on the design of the bridge itself, the health impact of an expansion has been largely overlooked.

"There is a human experiment unfolding in front of us," he says. "We are taking people who are already negatively impacted and we are going to make matters worse."



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Lwebuga-Mukasa further explains that increases in the prevalence and morbidity of asthma have been greatest in countries where there is more dependence on diesel fuel, which is used by trucks.

According to the UB study, patients living along Niagara Street, Seneca Street and Interstate 190, which are feeder roads for the Peace Bridge and therefore carry truck traffic, had increased odds of having asthma, while those living along routes that carry mostly automobile traffic, did not.

In their study, the UB researchers gathered data on two groups of patients who visited Buffalo's Millard Fillmore Hospital between 1996 and 2000: one included 3,700 patients who came to the hospital because of asthma, and the other included 4,000 control patients who came to the hospital for a condition completely unrelated to respiratory disease—gastroenteritis.

The authors then used geographic information science tools to conduct spatial analysis of hospitalization data.

The researchers acknowledge that because they were dealing only with hospitalization data, the study does not take into account other possible factors for the prevalence of asthma, such as exposure to indoor pollutants, age of housing and occupational exposures.

Lwebuga-Mukasa concludes that if the research community can find ways to mitigate truck-related pollutants, such strategies will have a positive impact not just in Buffalo, but in other communities struggling with the same phenomenon.

Currently, the UB researchers are collaborating with scientists from Columbia University and the Harvard School of Public Health in an effort to reach this goal.

Co-authors of the paper described above are Tonny Oyana, PhD, formerly a doctoral student in the Department of Geography in the UB College of Arts and Sciences, and Peter Rogerson, PhD, UB professor of geography. The research was supported by the Centers for Disease Control and Prevention and the Troup Fund, Kaleida Health Foundations. BP

Post-Rehabilitation Mortality

In a study published in the October 13, 2004 issue of *JAMA*, researchers at UB and the University of Texas Medical Branch found that although health insurance carriers reduced the number of treatment days covered in medical rehabilitation hospitals by nearly 40 percent during the past decade, this reduction didn't diminish treatment effectiveness. However, the analysis revealed a disturbing trend: Patients were not living as long after discharge from the hospitals.

By Lois Baker

To arrive at these finding, the researchers analyzed records of 148,897 patients treated in 744 inpatient medical rehabilitation hospitals in the U.S. between 1994 and 2001. They found that deaths between discharge and a six-month follow-up increased from less than 1 percent in 1994 to 4.7 percent in 2001.

Carl V. Granger, MD, professor in the Department of Rehabilitation Medicine in the UB School of Medicine and Biomedical Sciences and senior author on the study, says the increase in mortality over the study period was unexpected and needs to be monitored.

Researchers have no concrete explanations for the earlier deaths, he adds, and cautions about misinterpreting the study's results.

"We don't have enough data on other diseases, medical events and treatments that occurred either in the acute care hospital or in the rehabilitation hospital," says Granger. "Patients weren't randomly selected, so the data are subject to selection bias. In addition, this is the first time these data have been brought together and analyzed to this degree. Further analysis may produce different results.

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"There have been dramatic changes throughout health care over the past decade, and all the factors affected by these changes are not included in the databases we examined," he continues. "Plus, we don't know the settings in which patients died or how soon they died after rehabilitation hospitalization."

Granger emphasizes that this analysis includes data from rehabilitation hospitals only, because they routinely perform follow-up assessments after discharge. The outcomes for patients who received rehabilitation in other settings, such as home care, nursing homes, or outpatient clinics are unknown because they aren't monitored systematically.

Kenneth J. Ottenbacher, PhD, formerly of UB and now at the University of Texas Medical Branch, was first author on the study, which was supported by grants to him from the National Institutes of Health.

Data for the study were drawn from the Uniform Data System for Medical Rehabilitation (UDSMR) at UB. The UDSMR is the largest national registry of standardized information on medical rehabilitation in the U.S., and Granger was one of its founders in 1983.

Researchers on the study, in addition to Granger and Ottenbacher, are Sandra B. Illig and Pam M. Smith, DSN; Glenn V. Ostir, PhD, of the Sealy Center on Aging, University of Texas Medical Branch; and Richard T. Linn, PhD, of UDSMR and the UB Department of Rehabilitation Sciences.

To learn more about this study, visit the UB News Services' Web Site at http:// www.buffalo.edu/news/and search "Granger." BP

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Short, but Not Shorted

Rethinking when to prescribe human growth hormone

By Lois Baker

A new study counters the prevailing belief that children and adolescents who are extra short have social adjustment problems and fewer friends than children of average height, challenging one rationale for intervening at an early age with human growth–hormone treatment.*

In the first study of its kind conducted in a general population, researchers at the University at Buffalo assessed students across the full range of heights in the classroom setting. The students were unaware that height was a factor being studied. The study was conducted in grades six through 12 in a public school system in Western New York.

The findings, published in the September 2004 issue of *Pediatrics,* show that height plays no role in the number of friendships extra-short or extra-tall children have, the number of classmates who identified them as friends, their peer acceptance, height of their friends or their social adjustment in general.

The one characteristic associated with height was perceived age: Shorter students were thought to look younger than their age, but this association diminished in later grades.

"All of our current thinking concerning social adjustment problems associated with short stature is based on experiences of children and adolescents who come to pediatric endocrinologists for an evaluation of growth," says lead researcher David E. Sandberg, PhD, associate professor of psychiatry and pediatrics in the UB School of Medicine and Biomedical Sciences.

"Those receiving such an evaluation might not be representative of children who are just as short, or shorter, but who do not receive such an evaluation.

"To learn about the social experiences of youths with short stature, independent of whether they are being medically evaluated, we have to leave the clinic or hospital setting and move our research to the community. In that setting, we also can learn about the social adjustment of kids with short stature from those who have a lot to say about it—their peers," he says. "Peers are very good at identifying those among them who are likely to experience future mental-health or social problems."

Adolescence can be a stressful time for many children, Sandberg notes, and most children are teased or picked on. He says parents and clinicians should be careful not to misattribute significant social adjustment problems to height. By doing so, he cautioned, they may risk missing the true cause of the difficulties: Instead of addressing these factors, the child would be exposed to a long-term, invasive and expensive growth-hormone treatment that does not produce the desired social benefits.

Photo by: KC Kratt

David E. Sandberg, PhD, associate professor of psychiatry and pediatrics

The current study involved 965 students from 45 classrooms, all of which had at least one student with a height that fell at or below the fifth percentile for age and gender-specific norms. Students' social functioning was assessed through three types of questionnaires.

> Peers are very good at identifying those among them who are likely to experience future mental-health or social problems.

In the first, each student listed his or her best friends among their participating classmates. In the second, they rated each classmate on a five-point scale, from "don't like" to "like a lot." The third questionnaire contained a list of 28 personality characteristics, or "roles." The students were instructed to pretend they were casting a play, and were to select a person from both genders who best fit each of the 28 roles. They also were asked to select those roles for which they thought they were best suited.

The list included such roles as: "is a good leader," "loses temper easily," "has many friends" and "gets picked on."

This tool is designed to assess what a child is like in the eyes of peers, explains Sandberg.

Results of these assessments showed that student height was unrelated to how well students were liked by others, what others thought of them, their own perceptions of their reputation or their social adaptation within their peer group.

"Despite the social stereotypes that abound regarding the disadvantages of short stature, systematic research using sensitive tools to assess social adjustment provides little support for the notion that extremes of height—either short or tall—threaten healthy social adjustment," Sandberg states. "In other words, if significant problems of social adjustment are detected among short youths, then factors other than height should be considered as contributory."

Co-authors on the study are William M. Bukowski, PhD, of Concordia University; Carolyn M. Fung, program assistant in the UB Department of Psychiatry; and Robert B. Noll, PhD, of Children's Hospital of Pittsburgh, University of Pittsburgh.

The research described in this article was supported by the Human Growth Foundation, Genentech Foundation for Growth and Development, and Children's Growth Foundation. BP

**Although this study cautions physicians to rethink the use of growth hormone for extra short children to influence social adjustment, there are clear-cut medical indications for the use of human growth hormone in patients.*

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