Sexual Orientation and Cancer Risk

Young people in “sexual minorities” are at higher risk of cancer because they engage in risky behavior more often, according to researchers from City University of New York, Harvard University, Boston’s Children’s Hospital, and San Diego State University.

They analyzed data from 9,958 participants in the national Growing Up Today Study (1999–2010). The study participants were the children of the women in the Nurses’ Health Study II; those women were invited in 1996 to enroll their 9- to 14-year-old children. Of the participants, 84.5% reported being “completely” heterosexual, 12.1% were “mostly” heterosexual, 1.8% were lesbian or gay, and 1.6% were bisexual.

The researchers measured responses about tobacco and alcohol, diet and physical activity, exposure to ultraviolet radiation, and sexually transmitted diseases.

Lesbian, bisexual, and mostly heterosexual women more frequently engaged in multiple cancer-related risk behaviors, compared with completely heterosexual women. For instance, they were more likely to have smoked, to be overweight, and to have been physically inactive in the previous year. Bisexual and mostly heterosexual women were more likely to have had a sexually transmitted infection (STI). Interestingly, heterosexual women were more likely to have used a tanning booth 10 or more times in the previous year.

Sexual-minority women were also more often engaged in risky behaviors compared with men. The differences between gay/bisexual men and heterosexual men were less marked, although gay men more often vomited to control their weight, compared with heterosexual men, and had a higher prevalence of STIs.

The literature, the researchers note, tends to focus on “ever or never” behavior. They were mindful, they say, that exposure to a potential carcinogen usually must occur over time and that the likelihood of cancer increases with exposure, which is why they focused on assessing frequent engagement in each cancer-related risk behavior, long term. Their findings indicated that sexual minorities, relative to heterosexuals, are at risk for cancer through multiple risk behaviors—“concerning,” they add, because the “additive or synergistic effect of another cancer-related risk behavior may provoke or exacerbate a determinant of cancer: chronic inflammation.”


Unraveling the Genetic Mystery of Pneumocystis

National Institutes of Health researchers have sequenced nearly the entire genome of Pneumocystis, cause of one of the deadly infections that first defined the human immunodeficiency virus/acquired immunodeficiency syndrome epidemic. Pneumocystis is still a significant risk for those patients, as well as transplant recipients and other immunosuppressed patients.

Pneumocystis has puzzled researchers for years—especially how it developed its unique mechanisms of adaptation to life in mammals. “Having the genome information helped us recognize the unusual biology of Pneumocystis and how it coexists with its mammalian hosts,” said Liang Ma, MD, first author of the paper on the study. Through analysis, the researchers now better understand where the organism lives—it’s “highly adapted to existence in the host lung with strict dependence on the mammalian host for nutrients and a stable environment.” They can also get a better idea of how it avoids elimination by the host’s immune system.

The researchers say their study helps map out a clearer picture of the genomes, compared with prior studies, with high-quality, near-chromosomal draft genomes—the “highest level of genomic mapping.” That high quality helped them identify metabolic pathways critical to the growth and survival of the organism, as well as pathways in other closely related fungi that Pneumocystis does not have. The pathways likely disappeared as Pneumocystis evolved to become highly dependent on its host to stay alive, the researchers say.

Their detailed description of genes that are present or missing should facilitate attempts to culture the organism, they note. Culturing could help speed up drug development and even allow for genetic manipulation to modify the genes involved.

Source: National Institutes of Health, April 11, 2016

Treadmill Testing for Pulmonary Patients

Although treadmill tests that show lower resting heart rate, higher peak heart rate, and greater fitness can mean a more favorable prognosis, is that true for patients with obstructive lung disease? They share many risk factors with cardiovascular patients, and they have a high risk of developing—and dying from—cardiovascular disease. What’s more, some pulmonary medicines influence heart rate and raise the risk of adverse cardiovascular events in patients with chronic obstructive pulmonary disease. So researchers from Johns Hopkins in Baltimore, Henry Ford Medical Group in Detroit, and King Abdul-Aziz Cardiac Center in Riyadh, Saudi Arabia, conducted a study to determine whether the treadmill test parameters are actually useful in predicting outcomes for pulmonary patients.

The researchers compared 6,145 patients from the Henry Ford Exercise Testing Project (FTT) who were taking medications used to treat obstructive lung disease with 63,740 who were not taking such medicines. Patients were followed for a mean of 11 years.

The resting heart rate and peak heart rate parameters were “equally prognostic,” the researchers say. Exercise parameters achieved on the treadmill test were similar for patients in both groups. Higher fitness was associated with improved clinical outcomes in both groups, but the relative benefit to survival...
was even greater in patients taking pulmonary medicines. It's “clinically useful,” the researchers say, to know that the presence of underlying lung disease does not significantly affect the prognostic value of exercise treadmill testing.


**Improving Post-Stroke Outcomes With Endovascular Treatment**

Intravenous (IV) thrombolysis—standard treatment for acute ischemic stroke—improves functional recovery in only about one-third of patients, and recanalization rates are “not ideal,” say researchers from the University of Lisbon and Hospital de Santa Maria, Lisbon. Based on their meta-analysis of 10 multicenter randomized trials involving 2,925 patients, they suggest that adding mechanical endovascular reperfusion techniques may help improve clinical outcomes. However, they note, according to current research, the clinical benefits of adjunctive intra-arterial mechanical thrombectomy are uncertain.

The researchers aimed to compare endovascular treatment with standard medical care alone (particularly with IV recombinant tissue plasminogen activator [rt-PA]) in adults with ischemic stroke.

Overall, 39% of patients achieved a good functional outcome at 90 days. Those who received endovascular treatment had a higher chance of a good outcome, without increased mortality or symptomatic intracerebral hemorrhage. More than 86% of patients were treated with stent retrievers; in those cases, rates of recanalization were higher (more than 58%) than previously reported.

Adding thrombectomy to standard IV rt-PA “opens the conventional treatment window from 4.5 hours to at least six hours” in some patients, the researchers say—that is, patients younger than 85 years with strokes involving the large vessels of the anterior circulation where brain damage is not widespread and the intervention is performed within six to eight hours after an acute stroke. The best time to decide on adjunctive thrombectomy, they advise, is shortly after patients start to receive IV rt-PA.

In stroke trials, it is customary to provide outcomes at 90 days. But spontaneous neurological recovery may take longer to attain maximal potential, the researchers say, so longer follow-ups could have contributed to a better understanding of the evolution of functional endpoints through time.

Recommending endovascular treatment (particularly adjunctive intra-arterial mechanical thrombectomy with stent retrievers) as a new standard of care, the researchers note, requires a restructuring of comprehensive stroke centers and of interventional neuroradiologists’ training. However, they suggest cost-effectiveness analyses first to ascertain the value of endovascular thrombectomy before widespread implementation and restructuring.

Source: *BMJ*, April 2016

**Getting Closer to a Vaccine Against *C. Difficile***?

Could a vaccine help prevent infection with *Clostridium difficile*, which causes thousands of deaths every year? In a first-in-humans phase 1 study, researchers compared three doses of an investigational vaccine with placebo.

The vaccine consisted of toxoids A and B (the principle virulence factors of *C. difficile*-associated disease), given with or without aluminum hydroxide in doses of 50, 100, or 200 mcg at months 0, 1, and 6.

The vaccine was well tolerated and effective. Local reactions and systemic events—mostly injection-site pain, headache, and fatigue—were predominantly mild to moderate. Increasing the dosage or number of doses did not affect the frequency and severity of adverse effects, as reported by the participants in e-diaries.

Both the toxin A- and toxin B-specific neutralizing antibody levels increased from baseline. The first dose produced “modest” increases, but the second dose produced “marked” increases and the third dose had a “substantial” booster response, the researchers say. The booster response against toxin A was similar in both age groups tested (50–64 years and 65–85 years); the response against toxin B was the same or slightly higher in the older group.

Overall, antibody responses were higher in the toxoid-only groups. The researchers note that aluminum salts have been used to enhance vaccine responses for decades and it was “somewhat unexpected” in this study that the toxoid-only vaccine led to better antibody responses.

While the study was limited by the small number of participants, the researchers say, the robust response and persistence of immune response to 12 months support further investigation.

Source: *Vaccine*, April 2016

**Aprepitant Protects Against Chemo-Induced Nausea and Vomiting**

Patients on a cisplatin regimen are very likely to suffer chemotherapy-induced nausea and vomiting—more than 90% do, according to international guidelines. Antiemetic prophylaxis with a 5-hydroxytryptamine receptor-3 antagonist (5-HT₃,RA) plus dexamethasone still leaves about 20% of patients with acute or delayed vomiting and nausea during the first cycle of chemotherapy. However, researchers from Chang Gung University in Taiwan found that adding aprepitant provided about 70% complete protection against emesis when the primary prophylaxis didn’t work. Those findings led them to conduct a study evaluating the antiemetic efficacy of a combination of three drugs: palonosetron (a long-acting second-generation 5-HT₃,RA), three-day oral aprepitant (a neurokinin-1 receptor antagonist), and dexamethasone.

Patients in the study were scheduled to receive at least 50 mg/m² of cisplatin followed by a continuous infusion of 5-fluorouracil (5-FU) with or without other chemotherapeutic
agents. Cisplatin was given on day 1; the other drugs were given on day 1 and subsequent days. All 69 patients who received palonosetron, aprepitant, and dexamethasone were evaluated in the first cycle of chemotherapy.

No patients experienced acute vomiting; nearly all (98.6%) were protected against nausea. Moreover, 97.1% had no delayed vomiting, and 87% had no delayed nausea. Most episodes of delayed nausea were rated as mild. Overall, 97.1% of patients had no vomiting and 85.5% had no nausea.

The effects were sustained: In the second cycle of chemotherapy, again, none of 61 evaluated patients experienced acute vomiting and 96.7% were free of nausea. Most patients were also protected against delayed vomiting or nausea (96.7% and 83.6%, respectively). Of patients who underwent two cycles, 45 did not experience nausea or vomiting in either cycle.

The combination of drugs was generally well tolerated; most adverse events were mild.

Source: Biomedical Journal, February 2016

**Quick Screen for Adolescents At Risk for Alcohol Abuse**

One question—how often have you had a drink in the past year?—could be enough to identify a young person at risk for alcohol problems, according to a study funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

The study was conducted by University of Pennsylvania researchers, collaborating with practitioners at six rural primary care clinics in Pennsylvania. Using a computer-based questionnaire, they screened nearly 1,200 participants ages 12 through 20 years for alcohol use disorder (AUD).

The researchers found that in the past year, 10% of those over age 14 met the criteria for AUD outlined in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition. Adolescents between 12 and 17 years of age who reported drinking at least one standard drink on three or more days in the past year were at highest risk: 44% had AUD.

The three-day guideline had 91% sensitivity and 93% specificity. A negative screen (fewer than three drinking days in the past year) effectively ruled out AUD, with 99% not having the disorder.

For young people ages 18 to 20 years, the best screen was to ask whether they had engaged in drinking on 12 or more days in the past year. Of those who reported that level of drinking, 31% had AUD.

The researchers also assessed screening methods outlined in NIAAA’s *Alcohol Screening and Brief Intervention for Youth: A Practitioner’s Guide*, and found the guidelines to be effective screens for AUD. They concluded that screening for frequency of alcohol use, followed by a diagnostic evaluation for those who screen positive, would be a “simple, brief, and cost-effective clinical assessment procedure.”

“Primary care physicians are encouraged to screen adolescents for alcohol problems, yet many do not, citing time constraints and other issues,” said NIAAA Director George Koob, PhD. “This study demonstrates that simple screening tools such as those in NIAAA’s Youth Guide are efficient and effective.”

Source: National Institutes of Health, April 6, 2016

**Hypertension, Diuretics, and Hearing Loss**

Hypertension, which has been linked, inconsistently, to the risk of hearing loss, is often treated with diuretics. But thiazides have also been associated anecdotally with hearing loss, and small studies have found furosemide can cause hearing loss, although it’s usually reversible. To find out the real risk, researchers from the Massachusetts Eye and Ear Infirmary, Brigham and Women’s Hospital, Harvard University, and Vanderbilt University investigated the relationship between hypertension, diuretic use, and hearing loss in 54,721 women in the Nurses’ Health Study I.

The outcome measured was self-reported hearing loss. During 774,096 person-years of follow-up, 19,296 cases of hearing loss were reported, for a cumulative incidence of 35%.

About one-third of the participants had a history of hypertension, which was independently associated with a “modestly” higher risk of hearing loss.

Among women with hypertension, 18% were taking thiazide diuretics alone, 3% were taking furosemide alone, and 0.1% were taking both. Neither thiazide diuretic use nor furosemide use was significantly associated with the risk of hearing loss. In addition, the duration of drug use was not associated with risk of hearing loss.

Evidence about the relationship between high blood pressure and hearing loss is limited, the researchers say, but they note that the stria vascularis, which is located in the lateral cochlear wall and is responsible for sending auditory signals to the central nervous system, is particularly sensitive to events that compromise vascular supply.

Source: American Journal of Medicine, April 2016