

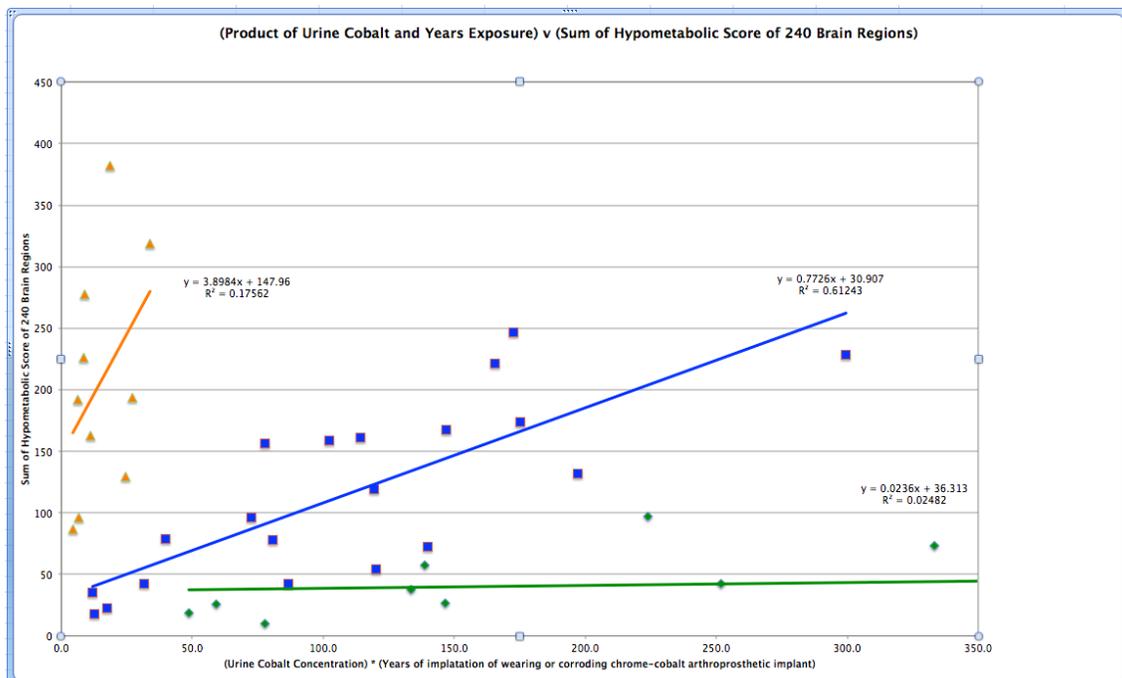


Update on Alaska Study of Arthroplastic Cobalt Encephalopathy (ACE) as of 7/25/18:

Dr. Tower's screening program of patients with an at-risk hip (patients with any chrome-cobalt part implanted within their body) began in March of 2015. This program now encompasses 161 patients; over half have been identified as having cobalt in their urine. Only a quarter of the patients with urine cobalt have the type of metal-on-metal hips known to be problematic, most have currently popular metal-on-plastic hips.

Of the patients identified with a urine cobalt presence, 81% of the 86 patients have 2 or more symptoms of ACE as opposed to only 19% of the 74 patients with no urine cobalt identified. This is a statistically significant finding ($p < 0.0001$). Forty of our urine cobalt patients without confounding neuropathology have undergone FDG-PET brain scans. All scanned patients show the same pattern of brain hypometabolism consistent with Chronic Toxic Encephalopathy (CTE). Other heavy metals, solvents, chemotherapeutic agents, and carbon monoxide also cause CTE. Our findings indicate that cobalt accelerates brain aging. The areas of the brain affected by CTE are notably different from those affected by Alzheimer's, Lewy Body, or frontotemporal dementias.

The FDG-PET brain scan is quantitative and is a sensitive measure of brain metabolism. Analysis of the data from our 40 scanned patients confirms that the severity of brain hypometabolism is a function of both the degree of cobalt exposure (concentration of cobalt in the urine) and the duration of exposure (number of years that the corroding/excessively wearing chrome-cobalt implant has been in place).



Notably, our scanned patients sort into three distinct clusters, relating to the patients' degree of sensitivity to arthroprosthetically generated cobalt as expressed by global and focal brain hypometabolism:

A quarter of patients (**the orange group on the graph**) are exquisitely sensitive, showing profound brain hypometabolism in response to a relatively low product of their urine cobalt concentration and the number of years implanted with a chrome-cobalt hip or shoulder implant.

In contrast, another quarter (**the green group on the graph**) are comparatively immune to the adverse effects of systemically circulated cobalt, showing only minor brain hypometabolism despite high urine cobalt levels and decades of exposure.

Half (**the blue group on the graph**) fall between. The slope of the regression lines shows that each group differs by an order of magnitude in degree of sensitivity to the ill effects of arthroprosthetically generated cobalt to its immediately adjacent group.

Collaterally, five patients were found with ACE whose shoulder replacements were the major sources of the patients' systemic cobalt. We have yet to identify a patient whose prosthetic knee is solely responsible for elevated urine or blood cobalt levels. However, prosthetic chrome-cobalt knee components may contribute to the elevated blood and urine cobalt levels in our patients who also have hip or shoulder chrome-cobalt arthroprosthetic components.

Most but not all of our patients whose ACE has been confirmed by brain imaging and who have undergone revision surgery to remove the source of systemic cobalt have improved neurologically within a year.

In a nutshell:

–One million Americans are at extreme risk for ACE from those metal-on-metal hip replacements that are no longer currently used, as well as from resurfacings. Most of these patients are not aware that they are at risk for systemic cobalt poisoning.

–5-10 million Americans are at indeterminate risk (likely varies by brand and model) for ACE from presently popular metal-on-plastic hips. Neither patients nor surgeons are aware of any potential for cobalt poisoning from nonmetal-on-metal hip replacements.

–One million Americans are at indeterminate risk for ACE from their replaced shoulders. Nearly all prosthetic shoulder systems employ modular chrome-cobalt implants. Patients and surgeons are unaware of the risk of cobalt poisoning from shoulder replacements.

–People fall into three markedly different groups concerning their sensitivity to the ill effects of arthroprosthetically generated cobalt: exquisitely sensitive, relatively immune, and an intermediate group. Each group is separated from one another by a ten-fold difference in dose/response to urine cobalt and duration of exposure.

–Attempts by various entities for over a decade to raise awareness of the risk of cobalt poisoning from chrome-cobalt implants have indicated that the industry has no issue with this problem.

In light of Dr. Tower's the above findings:

–Dr. Tower no longer implants any chrome-cobalt components because proven safe alternatives exist. He also monitors all of my patients already implanted with chrome-cobalt hip or shoulder parts with a yearly urine cobalt level. Those patients with a urine cobalt ≥ 1 part per billion (ppb) are queried about the symptoms of arthroprosthetic cobaltism as defined by the parameters of this study.

–Dr. Tower has noted that an FDG-PET brain scan is the study of choice to diagnose ACE. Dr. Tower recommends patients with more than two symptoms of 12 identified ACE symptoms and with a urine cobalt of ≥ 1 ppb get an FDG-PET brain scan. For those FDG-PET brain scans that confirm brain hypometabolism with the Chronic Toxic Encephalopathy pattern, Dr. Tower discusses the alternatives, risks, and benefits of revision arthroplasty to remove the source of the systemic cobalt.

–As noted previously above, due to Dr. Tower's decade of experience revising hips and shoulders for cobalt complications, his screening program suggests that most patients with ACE experience neurologic improvement within a year of revision surgery that is performed to exchange excessively worn or corroded/corroding chrome-cobalt components when exchanged for stainless steel, plastic, or ceramic alternatives. Six of his revised patients have shown improved brain metabolism on repeat FDG-PET brain scan within 6 to 2 months post revision, with noted documentation of a decline in urine cobalt levels. The two patients who deferred revision surgery have shown progression of brain hypometabolism 1-2 years after their index scan.