J Forensic Sci, March 2009, Vol. 54, No. 2
doi: 10.1111/j.1556-4029.2008.00973.x
Available online at: www.blackwell-synergy.com

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Toxicant Exposure and Mental Health—Individual, Social, and Public Health Considerations

ABSTRACT: Thoughts and moods are the result of biological processes; disordered thoughts and moods may be the result of disordered biological processes. As brain dysfunction can manifest with emotional symptoms or behavioral signs, the etiology of some mental health afflictions and some abnormal conduct is pathophysiological rather than pathopsychological. Various studies confirm that some chemical toxicants which modify brain physiology have the potential to affect mood, cognitive function, and to provoke socially undesirable outcomes. With pervasive concern about myriad chemical agents in the environment and resultant toxicant bioaccumulation, human exposure assessment has become a clinically relevant area of medical investigation. Adverse exposure and toxicant body burden should routinely be explored as an etiological determinant in assorted health afflictions including disordered thinking, moods, and behavior. The impact of toxicant bioaccumulation in a patient with neuropsychiatric symptoms is presented for consideration as an example of the potential benefit of recognizing and implementing exposure assessment.

KEYWORDS: forensic science, depression, environmental exposure, environmental medicine, mental status, mercury poisoning, neurotoxins, obsessive–compulsive, public health, toxicology

Extensive evidence in the recent medical literature confirms that individual and public health are being threatened by various chemical exposures. Recent publications are replete with mounting evidence of the dangers of adverse toxicants including neurotoxins that compromise normal development (1), endocrine disruptors that modify hormonal action (2), chemical mycotoxins with potential to suppress immune function (3), and industrial agents with myriad pathological mechanisms of harm including carcinogenicity (4). Through the use of a case history, the potential impact of toxicant exposure on one individual and the risk for those under his care is presented for consideration.

Breathing contaminated air, consumption of tainted food and drink, and dermal application of skin products containing synthetic chemicals are common sources of exposure to xenobiotics—chemical toxicants that are foreign to the human body. In the 21st century, the average individual in western culture is habitually exposed to numerous toxicants in their day-to-day lives as a result of myriad synthetic chemical products in homes, on playgrounds, in schools, in food establishments, and in workplaces. In response to this actuality, the Centers for Disease Control recently carried out the largest and most comprehensive analysis of toxicant exposure ever performed on humans and found that most American adults and children have bioaccumulated numerous potentially toxic chemicals including heavy metals (5). Similar studies in other nations, including Canada in 2006 (6), have also uncovered widespread toxicant contamination with various agents including mercury. The problem of chemical bioaccumulation is not limited to those directly exposed—most developing children are also at risk as a result of vertical transmission. A recent study of cord blood taken by the American Red Cross revealed that the average sample at birth already contained 287 toxicants including heavy metals, various pesticides, gasoline by-products, and fire retardants (7).

Assorted chemical agents have been found to affect physiological functioning and to induce disease in various organ systems. Cigarette smoke and air pollution, for example, are primary causes of respiratory illness (8), arsenic exposure has been associated with development of diabetes (9), various drugs and chemicals are well-recognized sources of liver dysfunction (10), and several toxicants are known to induce renal damage (11). History has also demonstrated, however, that certain chemicals can profoundly affect brain function and alter human emotion, thinking, and behavior. The implications for society of pathological behavior are significant; while bizarre behavior may immediately be recognized and addressed, subtle and insidious changes in thoughts and behavior may remain unnoticed with potentially serious outcomes.

It is well known, for example, that use of recreational chemicals such as alcohol and various street drugs can affect brain function with alterations in thinking and behavior. Assorted pharmaceutical agents can also alter brain chemistry and provoke pathological behavior—antivirals such as ribavarine and interferon, for example, can induce profound depression (12), and pediatric selective serotonin reuptake inhibitor (SSRI) use has been linked to aggression and self-destructive behavior in some cases (13). Recent evidence confirms that some other chemical agents found in the environment have the potential to induce pathological change in mental function.

Case History

A 24-year-old unmarried primary school teacher with complaints of fatigue, depression, and disturbed thinking was referred to a physician trained in environmental medicine. A detailed chronological history revealed that the patient last felt well about 24 months previously at which time he began to experience worsening depression, insomnia, and obsessive–compulsive tendencies. He also complained of increasing anxiety and frequent intrusive ideation of

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Received 26 Mar. 2008; and in revised form 2 May 2008; accepted 3 June 2008.

inflicting harm upon pupils within his elementary school class. Reluctant to disclose his thoughts to friends or family, he confided in a counselor and was immediately referred to a psychologist.

Various themes were explored in therapy including a troubled childhood, perceived sexual inhibition, and alleged spiritual conflicts. Despite intense therapy over many weeks, the thought fixation and mood lability persisted. Thinking he was ''demonized,'' the patient independently pursued spiritual guidance, a process which failed to ameliorate his symptoms; the religious advisor counseled him to consult a medical doctor. A family physician immediately instituted therapy with an SSRI antidepressant (fluvoxamine)—which, after 16 weeks of increasing doses made little difference to his depression or intrusive thoughts. Concern was expressed about the serious potential impact of persisting ideation to hurt children. With the potential for such ideation to be translated into actual behavior, a ''stress leave'' from work and a psychiatric consultation were arranged.

Psychiatric assessment and management failed to realize sustained benefit despite pharmacotherapeutic interventions including a second SSRI medication (paroxitene), a serotonin-norepinephrine reuptake inhibitor (SNRI) drug (venlafaxine), a tricyclic antidepressant (clomipramine), combination therapy of paroxitene and clomipramine, as well as augmentation therapy with antipsychotic medications (risperidone and olanzapine). In response to these drug therapies, however, the patient experienced assorted side effects including marked weight gain, persistent nightmares, debilitating drowsiness, and intractable constipation. With no family history of mental health problems, the patient questioned the ''inborn chemical imbalance'' label and was devastated to hear he had a chronic mental illness requiring lifelong medication. Suicidality became an increasingly prominent feature of his presentation.

Examination was unremarkable, but a detailed exposure assessment [developed by the Ontario College of Family Physicians (14)] followed by a red blood cell toxicological metal screen (15) revealed high levels of mercury, likely originating from his considerable intake of canned tuna. Three years previously, the patient read that essential fatty acid consumption through dietary fish was beneficial for brain function—information, which led to daily ingestion of one to two cans of tuna fish. With onset of depressive symptoms, his tuna intake increased by about 50% in response to a nutritionist recommendation that omega-3-fatty acids were therapeutic for mood disorders. Dietary history alongside recent World Health Organization reports identifying seafood as a leading cause of mercury exposure (16) provided the indication for metal screening.

In view of the patient's history of considerable ongoing tuna consumption and his associated laboratory findings, subsequent clinical discussion included options for detoxification of accumulated mercury as: (a) mercury is known to accumulate in brain tissue (17) and to act as a neurotoxin; and (b) blood levels of toxic metals (an indication of recent exposure) often underestimate mercury bioaccumulation within tissues (15). With avoidance of tuna and interventions to facilitate mercury removal including use of dimercaptosuccinic acid (18), the patient's psychiatric symptoms completely resolved within 8 months, the intrusive ideation disappeared, he discontinued all medication, and returned to work as a happy, productive young man.

Discussion

The phrase ''Mad Hatter Syndrome'' was initially used to describe a constellation of signs and symptoms including agitation, anxiety, melancholy, and personality changes that developed in workers occupationally exposed to mercury. The felt hat industry, dating back to 17th-century France, involved the application of a mercury compound to animal fur—a procedure involving the licking of brushes drenched with this toxic solution. After continued occupational exposure, the hatters often exhibited various psychiatric manifestations earning them the designation: mad hatters.

Mercury toxicity has been well documented in the recent medical literature (19,20). In Japan, for example, a petrochemical and plastic-maker company dumped an estimated 27 tons of mercury compounds into Minamata Bay from 1932 to 1968—thousands of people whose diet included fish from the bay developed symptoms of mercury poisoning. In Iraq, the consumption of wheat and barley seed sprayed with a mercury fungicide also led to considerable morbidity and mortality. As much current exposure to mercury occurs through the intake of contaminated seafood (21), concern has been expressed in the medical literature about the potential encephalopathic state induced by mercury and other brain toxicants (22).

In the general media, reports of mercury toxicity have also been discussed: the front page of the Wall Street Journal, for example, recently unveiled a story about a child afflicted with neurologic illness—after the case baffled various physicians, parental prompting followed by laboratory testing confirmed mercury intoxication (23). One-quarter of adult New Yorkers, roughly 1.4 million people, have elevated levels of mercury in their blood from fish consumption, according to a study released by the city's Department of Health and Mental Hygiene (24). The issue of mercury contamination has also prompted public health organizations such as Health Canada and the U.S. Food and Drug Administration to issue recommendations over the last few years to limit some seafood intake in vulnerable patient groups such as children and pregnant women because of potential toxicity (25,26).

Other chemical toxicants are also receiving considerable attention in recent scientific literature. *Environmental Research*, for example, published extensive evidence that pediatric exposure to lead is a profound determinant of criminal behavior (27). The study concludes that there is a strong association between preschoolers' blood lead levels and rates of heinous crimes such as murder, rape, aggravated assault, and burglary 19 years later—when the preschoolers grow up. Of further interest is the suggestion that lack of ability to rehabilitate such offenders with recidivist behavior may be related to persistent accrued toxicants and that epidemiologic declines in lead levels in several industrialized countries appear to correspond directly with later drops in crime rates (27). As well as serious crime, chemical toxicants may contribute to ubiquitous petty crime, aggressive behavior, as well as impaired school and social functioning. A report in *JAMA* suggests that teenage boys with higher than normal lead levels were more likely to engage in bullying, vandalism, arson, shoplifting, and other socially undesirable behavior than their nonlead exposed counterparts (28) and reports in the *New England Journal of Medicine* and other publications suggest that accrued lead can diminish intellectual function and school performance (29,30).

These reports highlight two important findings. First, exposures many years prior may be the source of stockpiled toxicants within the body and the source of ongoing adverse impact; the finding of accrued toxicants does not necessarily indicate recent exposure. Many lipophilic compounds, for example, accumulate within adipose tissue (the brain contains considerable fatty tissue), and some toxicant compounds persist in the body as a result of continued enterohepatic recirculation (31). Accordingly, precaution to avoid further exposure does not necessarily eliminate the body burden of toxicants—investigations to assess for accumulated toxicants and active detoxification interventions may be required to clear the

body. As toxicant bioaccumulation within tissues may not be detected by performing a standard blood or urine analysis, specialized laboratory investigations such as intracellular level determination or challenge testing may be required (15).

Second, with the recognition that human thinking and human behavior can be profoundly influenced by chemical exposure and resultant bioaccumulation, it is important to rule out recent adverse exposure or accrued toxicants as contributing factors to aggression, crime, sexual deviancy, and other disordered behavior. The implications for the penal system, the justice system, public educational systems, and health care delivery give evidence for the importance and clinical applicability of the emerging area of environmental medicine. From a public health perspective, it is also relevant to consider that toxicant exposure and stockpiling may occur more frequently among disadvantaged people residing in older, poorly maintained housing, and among some indigenous populations who rely heavily upon fishing for their sustenance.

Concluding Thoughts

Moods and thoughts are just as biological as digestion and respiration. As a physical organ, the brain may respond to physical determinants of disease with manifestations typical of brain pathology including depression, headache, compromised intellectual functioning, altered thinking and behavior, anxiety, and insomnia. Although symptoms related to brain dysfunction may present as emotional or behavioral in nature, the etiology of some mental health afflictions is pathophysiological rather than pathopsychological. In the face of toxic insult to the brain, psychotherapy and psychopharmacology may assist in coping but do not address the cause of the affliction nor restore optimal mental health. In an era marked by increasing exposure to neurotoxicants such as mercury (1), health practitioners should consider toxicological factors and incorporation of exposure assessment tools (14) when encountering patients with mental health complaints and socially disordered behavior. Precautionary avoidance of further exposure and interventions to eliminate toxicants from the body may result in marked improvement or complete recovery.

The medical literature has highlighted the increasing problem of chemical exposure and the resultant toxicant bioaccumulation as a primary determinant in various health afflictions (1,32,33). Adverse exposure to other injurious determinants including intense electromagnetic radiation (34) or biological agents such as mold and certain fungal by-products (3) have also been correlated with illness including mental health problems. Emerging environmental health recommendations have encouraged primary care practitioners as well as specialists to incorporate exposure assessment tools when the etiology of medical afflictions, including mental health disorders, remains uncertain (35).

The Centers for Disease Control has recently stated that "virtually all human diseases result from the interaction of genetic susceptibility and modifiable environmental factors" (36). As chemical exposure is a potent and potentially modifiable determinant, public health measures to address this concern should be explored. From a community health perspective, intervention by prevention through public education programs regarding toxicant avoidance, and legislative regulation regarding toxicant use may be worthwhile in an effort to diminish rates of illness and some socially undesirable sequelae.

Key Points

1. As cognition and mood are biological functions, alteration in physiological and biochemical processes within the brain have the potential to disrupt mentation with resultant behavioral and mental health sequelae.
2. Increasing evidence in the medical and scientific literature suggests that chemical exposure and resultant toxicant bioaccumulation are correlated with pathophysiology in neurological development and brain function.
3. Health professionals and other officials should consider toxicant exposure and adverse chemical accumulation as a potential determinant when individuals present with inexplicable mental health problems or disordered behavior.

References

1. Grandjean P, Landrigan PJ. Developmental neurotoxicity of industrial chemicals. Lancet 2006;368(9553):2167–78.
2. Crews D, McLachlan JA. Epigenetics, evolution, endocrine disruption, health, and disease. Endocrinology 2006;147(6 Suppl):S4–10.
3. Genuis SJ. Clinical medicine and the budding science of mold exposure. Eur J Int Med 2007;18:516–23.
4. Knox EG. Childhood cancers and atmospheric carcinogens. J Epidemiol Commun H 2005;59(2):101–5.
5. Centers for Disease Control and Prevention. Department of Health and Human Services. Third national report on human exposure to environmental chemicals. NCEH Pub. No. 05-0570 Atlanta: Georgia, 2005;1–475.
6. Neumann J, Winterton S, Lu J, Roja DED. Polluted children, toxic nation: a report on pollution in Canadian families. Published June 2006. http://www.environmentaldefence.ca/reports/toxicnationFamily.htm. Accessed on 8 October 2006.
7. Environmental Working Group. Body burden—the pollution in newborns: A benchmark investigation of industrial chemicals, pollutants and pesticides in umbilical cord blood. (Executive Summary) July 14, 2005. http://ewg.org/reports/bodyburden2/execsumm.php. Accessed on 16 September 2005.
8. Ho WC, Hartley WR, Myers L, Lin MH, Lin WS, Lien CH, et al. Air pollution, weather, and associated risk factors related to asthma prevalence and attack rate. Environ Res 2007;104(3):402–9.
9. Coronado-González JA, Del Razo LZ, García-Vargas G, Sanmiguel-Salazar F, Escobedo-de la Peña J. Inorganic arsenic exposure and type 2 diabetes mellitus in Mexico. Environ Res 2007;104(3):383–9.
10. Wang T, Shankar K, Ronis MJ, Mehendale HM. Mechanisms and outcomes of drug- and toxicant-induced liver toxicity in diabetes. Crit Rev Toxicol 2007;37(5):413–59.
11. Van Vleet TR, Schnellmann RG. Toxic nephropathy: environmental chemicals. Semin Nephrol 2003;23(5):500–8.
12. Kumar R, Gupta R. Hepatitis C and psychiatry. Australas Psychiatry 2007;15(2):163.
13. Sibbald B. Legal action against GSK over SSRI data. CMAJ 2004;171:23.
14. Marshall LM. Exposure history. In: The Ontario College of Family Physicians http://www.ocfp.on.ca/local/files/EHC/Exposure%20Hx%20Forms.pdf. Acccessed on 9 October 2006.
15. Bralley JA, Lord RS. Laboratory evaluations in molecular medicine: nutrients, toxicants, and cell regulators. Norcross, GA: The Institute for Advances in Molecular Medicine, 2005.
16. Bigham M, Copes R, Srour L. Health Canada: exposure to thimerosal in vaccines used in Canadian infant immunization programs, with respect to risk of neurodevelopmental disorders. Table 1—Estimated daily intake and retention of elemental and mercuric compounds in the general population not occupationally exposed to mercury. Can Commun Dis Rep 2002;28:69–80.
17. Guzzi G, Grandi M, Cattaneo C, Calza S, Minoia C, Ronchi A, et al. Dental amalgam and mercury levels in autopsy tissues: food for thought. Am J Forensic Med Pathol 2006;27(1):42–5.
18. Ozuah PO. Mercury poisoning. Curr Probl Pediatr 2000;30(3):91–9.
19. Clifton JC. Mercury exposure and public health. Pediatr Clin North Am 2007;54(2):237–69.
20. Counter SA, Buchanan LH. Mercury exposure in children: a review. Toxicol Appl Pharmacol 2004;198(2):209–30.
21. Sehmer J. Mercury in seafood. CMAJ 2002;167(2):122–4.
22. Eicher T, Avery E. Toxic encephalopathies. Neurol Clin 2005; 23(2):353–76.
23. Waldman P. Mercury and tuna: U.S. advice leaves lots of questions. Wall St J: August 1, 2005, p A1.

24. Cardwell D. High mercury levels found in one-fourth of adults. New York Times 2007; http://www.nytimes.com/2007/07/24/nyregion/24mercury.html?_r=2&adxnnl=1&oref=slogin&pagewanted=print&adxnnlx=1185627272-h4ZOq/vEX+ukZz8c2snopw. Accessed on 27 July 2007.
25. Health Canada. Health Canada advises specific groups to limit their consumption of canned albacore tuna. 2007; [http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_14_e.html. Accessed on 27 July 2007.
26. US Department of Health and Human Services UEPA. What you need to know about mercury in fish and shellfish. EPA and FDA advice for women who might become pregnant, women who are pregnant, nursing mothers, and young children. 2004; http://www.cfsan.fda.gov/~dms/admehg3.html. Accessed on 9 March 2007.
27. Nevin R. Understanding international crime trends: the legacy of preschool lead exposure. Environ Res 2007;104(3):315–36.
28. Needleman HL, Riess JA, Tobin MJ, Biesecker GE, Greenhouse JB. Bone lead levels and delinquent behavior. JAMA 1996;275(5):363–9.
29. Needleman HL, Gunnoe C, Leviton A, Reed R, Peresie H, Maher C, et al. Deficits in psychologic and classroom performance of children with elevated dentine lead levels. N Engl J Med 1979;300:689–95.
30. Nevin R. How lead exposure relates to temporal changes in IQ, violent crime, and unwed pregnancy. Environ Res 2000;83(1):1–22.
31. Jandacek RJ, Tso P. Factors affecting the storage and excretion of toxic lipophilic xenobiotics. Lipids 2001;36(12):1289–305.
32. Genuis SJ. The chemical erosion of human health: adverse environmental exposure and in-utero pollution—determinants of congenital disorders and chronic disease. J Perinat Med 2006;34:185–95.
33. Dumont MP. Psychotoxicology: the return of the mad hatter. Soc Sci Med 1989;29(9):1077–82.
34. Genuis SJ. Fielding a current idea: exploring the public health impact of electromagnetic radiation. Public Health 2008;122:113–24.
35. Weir E. Identifying and managing adverse environmental health effects: a new series. CMAJ 2002;166:1041–3.
36. Office of Genomics and Disease Prevention: Centers for Disease Control and Prevention. Department of Health and Human Services. Gene-environment interaction fact sheet. Washington, DC: Centers for Disease Control and Prevention, 2000.

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