Health hazards in the built environment and their relationship to childhood neurobehaviourhal disorders – Part 1

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In the past 20 years, the incidence of childhood neurobehavioural disorders such as autism and ADHD have increased worldwide[1] In the 1970s, autism was estimated to affect up to 5 in 10,000 children[2], now it is 1 in 68 US children[3]. Whilst the incidence of autism in Australia is lower (1:100) according to Autism Spectrum Australia[4] disturbingly it has increased by 79% between 2009 and 2012[5]. Better diagnosis and reporting cannot account for this rapid rise, nor can genetics, as none of the genes discovered so far seem to be responsible for more than a small proportion of cases[6]. Emerging evidence suggests the environment is likely to play a crucial role[7]. The dramatic increase in autism spectrum conditions has occurred coincidentally with the deployment of wireless technologies and shows remarkable similarities to the pathophysiology following exposure to radiofrequency electromagnetic fields[8]. In addition, a growing number of industrial chemicals have been identified as neurodevelopmental toxicants[9]. Since 2006, the number of chemicals known to damage the human brain that are not regulated to protect children's health increased to 214[10]. Research conducted by Lintas et al (2012)[11] identified immune genes and not neurodevelopmental genes as the most consistent abnormality typically found in neurodevelopmental disorders. An additional finding that further supports the environment as a contributing factor is the 'good and bad days' observed by parents and the transient reversal of symptoms in some children during fever[12] and short term antibiotic treatments[13], all of which question the premise that autism is a disease due to a 'broken brain'.

Developmental Neurotoxicants

Since WWII, thousands of chemicals have been introduced into building materials and consumer products. Since 1970, the global sale of chemicals has increased by a factor of 25 from $171 billion to $4.1 trillion US dollars and this is expected to accelerate[14]. It is estimated that 84,000 chemicals are used commercially[15], 38,000 of which listed for use in Australia[16]. Consequently the body burden of chemicals is increasing with each generation. There is strong evidence that industrial chemicals are contributing to a global pandemic of neurodevelopmental disorders which affect millions of children worldwide, the implications of which have devastating consequences on families and the global economy[9,17]. Despite this, neurodevelopmental toxicity data are missing for most industrial chemicals in widespread use, even when population wide exposures are documented[18]. Since 2006, eleven industrial chemicals have been identified as developmental neurotoxicants: lead, methylmercury, polychlorinated biphenyls, arsenic, toluene, manganese, fluoride, chlorpyrifos, DDT, tetrachloroethylene and polybrominated diphenyl ethers with many more likely to be discovered[10]. Some like lead and mercury have extensive documented histories of adverse health effects in children dating back to Roman times; others like pesticides, flame retardants and industrial solvents and lubricants have gained notoriety because they are ubiquitous throughout the environment, they bioaccumulate up the food chain and are biologically persistent having been found extensively in wildlife and in most of the general population[19]. Three are listed as persistent organic pollutants in the Stockholm Convention and all of them are listed as potential endocrine disrupting chemicals on the TEDX List (Endocrine Disruption Exchange, 2014)[20].

Flame retardants

Since the 1970s, flame retardants have been used in consumer products to reduce the likelihood that an item will ignite, inhibit the spread of a fire, and to provide occupants more time to escape from a fire. They have been incorporated into paints, children's clothing (low fire danger pyjamas), foams used in upholstered furniture, carpet padding, pillows and mattresses, as well as in plastic housings for televisions, computers, telephone handsets, power point fronts, light switches and kitchen appliances[21]. Consequently the levels of flame retardants are greater indoors than outdoors and higher in buildings that have recently been renovated, carpeted or are air conditioned[21]. Brominated flame retardants (also referred to as polybrominated diphenyl ethers or PBDEs) are the most

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common flame retardants found in households, eighty of which are used commercially in Australia[21]. PBDEs are a group of more than 200 distinct chemicals that are structurally similar to polychlorinated biphenyls[22]. The three types used commercially are pentaBDE, octaBDE and decaBDE each of which contains a mixture of congeners of PBDEs. Globally, decaBDEs are the most widely used brominated flame retardants as they are incorporated into wiring insulation, television and computer casings[23].

PBDEs have gained notoriety amongst the scientific community because their bioaccumulative and persistent nature, in addition to their endocrine disrupting effects, has adverse health outcomes in animals and humans[24]. Consequently tetraBDE and pentaBDEs are listed as persistent organic pollutants in the Stockholm Convention[25]. Prenatal and childhood exposures to PBDEs in both human and animal studies resulted in increased hyperactivity, lower IQ and significant deficits in learning and memory[26-29]. The mechanism of action is likely to be via its thyroid disrupting effects[30] although a smaller number of studies have also examined disruption of the oestrogen/androgen hormone system[31]. That's a concern in light of the fact that the levels of PBDEs measured in the breast milk and blood of Australians is twice as high as those found in Europeans[32-33] although it is lower than that found in Californian children who have the highest levels as a result of their fire safety law[28]. Since PBDEs are semivolatile, they are not chemically bound to the substrate material which is why they are commonly found in household dust which accounts for 80% of the total exposure to PBDEs in infants as compared to only 14% in adults[34]. As a result of this, blood concentrations of PBDEs in children is considerably higher than those found in adults[34]. Inhalation and ingestion of household dust is likely to be the most common route of exposure which makes young children particularly vulnerable[35]. The European Union has consequently mandated the phase out of certain PBDEs. Whilst NICNAS has banned the import and manufacture of two brominated flame retardants - pentaBDE and octaPBDE, it has not restricted their use in imported products (where children are most likely to be exposed), relying instead on a decline of these chemicals from voluntary activity by industry and to the lack of commercial availability as a result of international regulatory action[36]. At the same time, they insist that "there is no evidence of any adverse health effects in newborns, children or adults from exposure to PBDEs"[36]. In light of recent evidence associating prenatal and early childhood exposure to PBDEs with a decline in IQ and increased hyperactivity[29,37], assumptions of safety can no longer be taken for granted.

Lead

Lead has a long history of adverse health effects dating back to Roman times. Unlike other developmental neurotoxicants, it is the most common and best understood childhood disease of toxic environmental origin that accounts for 0.6% of the global burden of disease[38]. The deleterious effects of blood lead levels above10 ug/dL on brain function are well documented and include lowered intelligence and behavioural problems[39-42]. At lower levels of exposure that previously were considered safe, lead is now known to produce a spectrum of injury across multiple body systems[43]. A growing number of studies have shown that levels lower than 10 ug/dl are associated with adverse health effects such as inattention[44], cognitive loss[45-46],Attention Deficit Hyperactivity Disorder[47], reduced IQ and increased antisocial behaviour[43] and delays in sexual maturation in adolescent girls and boys[46]. The mechanism of action involves demyelination of neurons, death of brain cells, and disruptive effects on the dopaminergic system[48]. Many are questioning as to whether there are any 'safe' blood lead levels[43]. Consequently Germany has lowered its action level to 3.5 ug/dl, the US Centers for Disease Control to 5 ug/dl, and the NHMRC is currently reviewing Australia's action level currently set at 10 ug/dl. Australian children are especially at risk as it is estimated that 3.5 million homes contain paint with 50% lead content which is just one of several sources of lead in the environment[49]. An Australian national survey of lead in 1,575 children found an average of 5 ug/dl in 1 to 4 year olds (7% exceeded 10 ug/dl) although this was conducted before leaded petrol was phased out in 2002[50-51]. Nonetheless, inhalation and ingestion of house dust containing leaded paint remains a common source of exposure in young children.

Pesticides

The adverse health effects arising from pesticide exposure gained worldwide attention when Rachel Carson documented the abnormal mating behaviour in bald eagles and the collapse of the eagle population that were exposed to high levels of DDT in her book Silent Spring[52]. Organochlorine pesticides (OC) such as DDT, dieldrin, aldrin, heptachlor and chlordane were used extensively in Australia during the 1950s to mid-1970s, but were subsequently phased out by 1990 following serious adverse health effects in animal and human studies and because they persist in the environment. They were replaced with the organophosphate pesticides (OP) which are widely used in agriculture primarily because their half-life is significantly shorter. Approx. 5,000 tonnes of OP are used annually in Australia[53].

Whilst data associated with acute and/or accidental poisonings of pesticides in children is readily available, little data is available on subclinical pesticide exposure despite the fact that it is so widespread[10]. In 1998, Australian doctors at Townsville Hospital tested the meconium of 46 newborn babies and found a wide

range of hazardous chemicals including POPs and pesticides such as chlorpyrifos[54]. Data which describes the full, or even partial, extent of human health effects from exposure to pesticides is difficult to source due to potential long latency periods for chronic illness, the difficulty in diagnosis, the non-specific nature of pesticide health effects and the lack of effective monitoring systems[55]. Three prospective epidemiological birth cohort studies provide new evidence that prenatal exposure to OP pesticides can cause developmental neurotoxicity[56-58]. More recently, the Childhood Autism Risks from Genetics and Environment (CHARGE) study identified that children with ASD were 60% more likely to have organophosphates applied near their home, whilst children with developmental delays were 150% more likely to have carbamate pesticides applied near the home during pregnancy[59]. The mechanism of action is likely to be due to the fact that these pesticides are inhibitory neurotransmitters which are necessary in the development and maintenance of neuronal transmission. Prenatal exposure to OP pesticides in animal studies have demonstrated more severe neurodevelopmental effects for males than for females, suggesting endocrine disruption maybe involved[60]. Other classes of pesticides including the carbamates and the synthetic pyrethroids have also been linked to neurodevelopmental deficits in children[59,61-62].

Children are more vulnerable to pesticides because they receive a larger dose per unit of body weight for a given exposure due to their smaller body size[63], their unique diet (pureed fruit, vegies…), their breathing zone is closer to the floor, and the enzyme involved in detoxification - paraoxonase-1 (PON-1) is less active making them more vulnerable to OP toxicity[64]. Children are exposed to pesticides through inhalation (household dust, spraying), ingestion (food, drinking water and accidental poisoning) and dermal absorption (lice and scabies treatment, insect repellants, lawn, household dust…). Levels of pesticides in carpet dust can be useful indicators of exposure in epidemiologic studies, particularly for young children who are in frequent contact with carpets[65]. Pesticides may persist for long periods of time inside the home, where they are protected from degradation by sunlight, rain, temperature extremes, and microbial action[66]. Carpets are repositories for pesticides[67-68] as the fibres and underlying foam pad appear to act as long-term reservoirs that continuously transfer pesticides to carpet dust.

Endocrine disrupting chemicals (EDCs)

All of the neurodevelopmental toxicants highlighted by Grandjean and Landrigan (2014)[10] are listed as potential endocrine disrupting chemicals (EDCs) on the TEDX List (Endocrine Disruption Exchange, 2014). EDCs pose an additional concern for the unborn foetus and children because unlike other chemicals, their impact on cognition and behaviour is likely to arise at low levels of exposure during critical windows of development[1]. EDCs may well provide a vital clue as to why males are up to five times more likely to develop autism than females as highlighted by a recent spatial incidence study involving one third of the entire US population using insurance claims datasets. The authors concluded that the strongest predictors for autism were associated with the environment, as autism incidence was strongly linked to congenital malformations of the reproductive system in males which are not typically associated with genetic causes (an increase in autism incidence by 283% for every per cent of increase in the incidence of malformations)[69]. The incidence of genital malformations such as cryptorchidism and hypospadias has increased in recent times. The prevalence of hypospadias rose 2% every year between 1980 and 2000 in Western Australia[70] and similar trends were seen in South Australia[71] but not in Victoria or NSW. These malformations typically arise during early embryonic development – specifically between weeks 9 to 12 which corresponds to the time when cell division and migration takes place in brain development[72]. Coincidentally it is also the time when maternal exposure to xeno-oestrogens in animal models affects both the brain and genital development in male progeny[72]. Xeno-oestrogens are found in a number of environmental toxins including (but not limited to) OP pesticides, polybrominated flame retardants and polychlorinated biphenyls. A study published in 2007, identified that babies born with cryptorchidism or hypospadias had a more than 2.5 fold increased risk of having detectable levels of DDT and its metabolite DDE, lindane and several other organochlorine pesticides in their blood[73]. Some researchers have explained the gender bias seen in autism as a result of the fact that the female brain requires more extreme genetic alterations than does the male brain to produce symptoms of neurodevelopmental disorders (not related to the X chromosome)[74]. Gender bias is present in several neurodevelopmental disorders including autism, intellectual disability, and attention deficit hyperactivity disorder.

Part 2 will appear in the March 2015 Journal.

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