3rd May 2016 Redacted

Dr Simon Ridley

Alzheimer's Research UK

c/o reception@alzheimersresearchuk.org

Dear Dr Ridley,

Lead and Alzheimer's Disease?

I noted with interest your pieces on BBC News regarding a study which found a correlation between worsening depression and Alzheimer's Disease (AD). I see that Dr M Arfan Ikram stated that 'depression and dementia may both be symptoms of a common underlying cause' and that Dr Simone Reppermund stated that 'more studies were needed to understand the link'. I would like to suggest that it may be useful to encourage studies to examine the hypothesis that life-long exposure to lead may be that underlying cause.

A link between lead and AD has been suggested (J Wu et al 2008, Ref 1; Monnet-Tschudi, Zurich MG, Boschat C, Corbaz A, Honegger P. 2006, Ref 2). Another study showed a correlation between elevated, but 'safe', blood lead levels and psychiatric disorders including major depressive disorder (Maryse Bouchard et al, 2009, Ref 3 ).

It is known that lead from environmental or incidental exposure is stored in the bones (Holstege et al, 2015, Ref 4). Blood lead levels have been shown to increase through release from the bone after menopause (Vahter, Berglund M, Akesson A. 2004, Ref 5) and through loss of bone density (Nash D, Magder LS, Sherwin R, Rubin RJ, Silbergeld EK., 2004, Ref 6). It has also been explained that bone resorption can release stored lead and result in toxicological pathology (Pranay Kathuria, MD, 2016, Ref 7). Relationships between low bone density and depression have been found (G. Cizza, S. Primma, M. Coyle, L. Gourgiotis, and G. Csako, 2010 Ref 8). Furthermore, it is postulated that osteoporosis and AD may have common risk factors (Tysiewicz-Dudek M, Pietraszkiewicz F, Drozdzowska B., 2008, Ref 9).

The hypothesis therefore links the evidence into a chain from life-long lead exposure, to bone accumulation, to loss of bone density, to elevated blood lead levels and thence to neurotoxic effects including depression and AD. As a lay observer it seems to me that there is sufficient evidence to suggest that lead is causing at least some of the burden of AD and that further research is essential with potentially massive returns on investment in both relief of misery and care costs.

In the mean-time, it would appear that the effects of accumulated lead can be mitigated through exercise to maintain bone density (Chilibeck PD, Sale DG, Webber CE, 1995, Ref 11) and diet to maintain healthy bones (Cashman KD,

2007, Ref 12) and to chelate the lead (Qixiao Zhai, Arjan Narbad, and Wei Chen 2015, Ref 13) presumably including that released from endogenous poisoning. These behaviours are already included the recommended life-style changes published by Alzheimer's Research UK (Ref 10) to help reduce the risk of AD. If the lead hypothesis is correct then this could explain why good diet and exercise reduce the risk of AD, and many other conditions.

Myself and a couple of associates are developing the idea of charitable campaign to promote enhanced management, publicity and research in the UK with regard to the risk from lead and would like to ask whether you would be willing to provide your endorsement of this campaign. I would add that studies have shown correlations between blood lead levels, within the UK normal range, and a number of other conditions including stroke, coronary heart disease, peripheral arterial disease, ADHD, kidney disease and panic disorder. We believe that that the continued impact of lead on public health is grossly unrecognised in the UK, but that this can be addressed through appropriate actions at personal, professional and governmental levels.

Yours sincerely,

Redacted

References

Ref 1. Jinfang Wu, Md. Riyaz Basha, Brian Brock, David P. Cox, Fernando Cardozo-Pelaez, Christopher A. McPherson, Jean Harry, Deborah C. Rice, Bryan Maloney, Demao Chen, Debomoy K. Lahiri, and Nasser H. Zawia. Alzheimer's Disease (AD)-Like Pathology in Aged Monkeys after Infantile Exposure to Environmental Metal Lead (Pb): Evidence for a Developmental Origin and Environmental Link for AD'. *The Journal of Neuroscience,* Jan. 2, 2008; vol 28: pp 3-9

Ref 2. Monnet-Tschudi F1, Zurich MG, Boschat C, Corbaz A, Honegger P. Involvement of environmental mercury and lead in the etiology of neurodegenerative diseases. *Rev Environ Health.* 2006 Apr-Jun;21(2):105-17.

Ref 3. Maryse Bouchard, PhD, MSc, David C. Bellinger, PhD, MSc, Jennifer Weuve, MPH, ScD, Julia Matthews-Bellinger, PhD, MD, Stephen E. Gilman, ScD, Robert O. Wright, MD MPH, Joel Schwartz, PhD, and Marc G. Weisskopf, PhD. Blood lead levels and major depressive disorder, panic disorder, and generalized anxiety disorder in U.S. young adults. *Arch Gen Psychiatry.* 2009 Dec; 66(12): 1313–1319.

Ref 4. Christopher P Holstege, MD, J Stephen Huff, MD, Adam K Rowden; Chief Editor: Tarakad S Ramachandran.l Pathophysiology and Etiology of Lead Toxicity. *Medscape* 2015 Dec.

Ref 5. Vahter M, Berglund M, Akesson A., Toxic metals and the menopause. *J Br Menopause Soc*. 2004 Jun;10(2):60-4.

Ref 6. Nash D, Magder LS, Sherwin R, Rubin RJ, Silbergeld EK. Bone density-related predictors of blood lead level among peri- and postmenopausal women in the United States: The Third National Health and Nutrition Examination Survey, 1988-1994. *Am J Epidemiol*. 2004 Nov 1;160(9):901-11.

Ref 7. Pranay Kathuria, MD. Lead Nephropathy. *Medscape* 2016 January.

Ref 8. G. Cizza, S. Primma, M. Coyle, L. Gourgiotis, and G. Csako. Depression and Osteoporosis: A Research Synthesis with Meta-Analysis. *Horm Metab Res*. 2010 Jun; 42(7): 467–482.

Ref 9. Tysiewicz-Dudek M1, Pietraszkiewicz F, Drozdzowska B. Alzheimer's disease and osteoporosis: common risk factors or one condition predisposing to the other? *Ortop Traumatol Rehabil.* 2008 Jul-Aug;10(4):315-23.

Ref 10. Alzheimer’s Research UK. Reducing the risk. July 2015.

Ref 11. Exercise and bone mineral density. Chilibeck PD, Sale DG, Webber CE. *Sports Med*. 1995 Feb;19(2):103-22.

Ref 12. Diet, nutrition, and bone health. Cashman KD. *J Nutr*. 2007 Nov;137(11 Suppl):2507S-2512S.

Ref 13. Dietary Strategies for the Treatment of Cadmium and Lead Toxicity. Qixiao Zhai, Arjan Narbad, and Wei Chen 2015. *Nutrients*. 2015 Jan; 7(1): 552–571.