

4th International Conference and Exhibition on **Pharmacovigilance & Clinical Trials** August 10-12, 2015 London, UK

Over a century of Alzheimer and still no cause in sight: Is pharmacovigilance asleep on the job?

G Robert Jones

Cancer Research Unit, UK

Although Alzheimer's disease (AD), initially of rare idiopathic origin and characterized by Pinel in 1800 as chronic dementia, is now a major threat to global health, the number of publications pointing to an iatrogenic case remains in single figures. In 1971 Murray associated the typical lesions of AD with high lifetime intakes of phenacetin by kidney dialysis patients. The gradual replacement of the analgesic by paracetamol, its chief metabolite, and its removal from the UK pharmacopoeia in 1974 failed to check the exponential rise in patient numbers, not until 2001 was the suggestion made that the metabolite is also a risk factor. Phenacetin first went on open sale in 1887; its nephrotoxicity was reported in the following year. Chronic dementia was rediscovered by Fischer and Alzheimer in 1901, and given a new name in 1910. Significantly, the earliest cases displayed kidney damage ranging from nephritis to organ atrophy. The cunning abilities of AD to obliterate memory and to masquerade as senility with varying degrees of success, as well as the long silent period elapsing between analgesic exposure and the overt expression of symptoms, have together contributed to the failure to recognize a pharmacological cause. There is no evidence to support the widespread belief that the rising incidence of AD is a consequence of increasing longevity. Missed opportunities will be described and discussed.

Biography

G Robert Jones graduated in Natural Sciences from the University of Cambridge, and studied respiratory enzymes in cancer for his PhD in London. Working in London, Munich and the German Cancer Research Center in Heidelberg; he discovered that mitochondrial energy production provides the optimum target for cancer chemotherapy. His long and patient search for a humane, inexpensive and safe form of cancer chemotherapy is described in the book *Subjugation of Cancer (2010)*. In 2001 he discovered that Tylenol is a major risk factor for Alzheimer's disease.

darkshad@hotmail.co.uk

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