



# Risk factors for dementia

## What are risk factors?

For some diseases a definite cause is known. This is especially true for infections like measles, malaria or flu. However the situation is more complicated for many illnesses, particularly those which develop over a long period of time (such as heart disease, cancer or dementia). A person's chances of being affected may be influenced by many different factors, known and unknown, which may interact together in complex ways. None of these 'risk factors' may be enough in itself to cause the disease. For example, not everyone who smokes develops heart disease and not everyone with heart disease has been a smoker. However smoking is still a strong risk factor for heart disease.

## Why study risk factors in dementia?

Approximately 25% of people aged over 85 have dementia. Seventy five percent do not. Is this just a matter of pure chance or are there aspects of a person's genetic make-up or previous experiences in life which may affect the person's likelihood of developing dementia? These questions form the basis for risk factor studies. Some risk factors can be reduced in size and some protective factors can be increased. Other factors will not, by their nature, be open to modification.

## How are possible risk factors identified?

There are two different ways of identifying risk factors for disease. One is to compare groups of people with or without the disease in question – perhaps examining them, or taking a blood test, or asking them about previous events or illnesses. This is perhaps the most easily conducted type of study and is sometimes called a 'case control study'. If something is found more commonly than expected in people with the disease, this may be a risk factor. However it can sometimes be difficult to interpret results. In particular, people with a disease (or their relatives) may be more or less likely to remember past events than those without illness. Also, for a condition like dementia which may develop over a long period of time, people's lifestyles may

have changed because of the early stages of disease before a diagnosis was made.

An alternative way is to follow over time groups of people who do or do not have a suspected risk factor (for instance smokers and non-smokers). The risk of developing a particular disease (for instance heart disease or lung cancer) can therefore be compared between the groups. This is sometimes called a 'cohort study' and may provide more clear results. However these studies are usually much more costly and difficult to carry out, particularly if many years of follow-up are needed.

## What is known about risk factors for dementia?

Many different factors have been suggested to have an effect on risk of dementia. Some are risk factors, some appear to be protective. Many have not been fully established, meaning that some studies disagree in their findings and research is currently in progress to clarify the situation. 'Dementia' is a general term for progressive decline in higher brain function such as memory, concentration, and reasoning. Alzheimer's disease is the most common cause of dementia but other factors also contribute such as small strokes. These have traditionally been categorised into distinct disorders but there is a growing body of evidence which suggests that dementia in many cases is caused by mixed, overlapping processes which cannot easily be separated. Some risk-factor studies have been carried out for dementia as a whole whereas others have focussed on Alzheimer's disease as one particular disorder and this factsheet attempts to keep this distinction in discussing research findings. Listed below are risk factors currently being researched:

**Age.** Dementia may occur at any age but is very rare below the age of 60. Dementia becomes more common with increasing age, occurring in around 1% of people aged 65-69 but in around 24% of those aged 85 or older. Prevalence studies are described in more detail in *Factsheet 3*. It is still not known, however, whether increased rates of dementia with age are simply caused by the brain becoming older or whether they are because of other diseases or events which become more common in later life.

**Sex.** Most research shows no difference between men and women in the overall prevalence of dementia. However, some studies show that women have a slightly higher chance of developing Alzheimer's disease than men, after taking into account the fact that women live longer. Conversely, men have higher rates of stroke-related dementia.

## Family history and genetic factors.

Very rarely dementia may occur in people aged below 60, and this is often passed on as a clearly inherited disease. Also the majority of people with Down's syndrome who survive to late adulthood develop Alzheimer's disease, probably because of genetic differences. The role of genetic factors in late-onset dementia (dementia developing after age 60) is less clear. First degree relatives (children, brothers or sisters) of a person with Alzheimer's disease are three to four times more likely to develop this over a lifetime compared to someone with no affected relatives.<sup>1</sup> Similarly relatives of people with Down's syndrome or Parkinson's disease have a higher than average risk (about a threefold increase). One gene, apolipoprotein E (APOE) has been found to affect risk of future Alzheimer's disease in studies of large populations. People with the 'at risk' form of this gene are about three to four times more likely to develop Alzheimer's disease in their lifetime than those without. However effects of any of these factors on an individual are quite small. Most people with a positive family history or the APOE risk gene will not develop Alzheimer's disease. Also most people with Alzheimer's disease do not have an identifiable genetic risk. Genetic factors in Alzheimer's disease are covered in detail in *Factsheet 6*.

**Education.** Many studies show that dementia, and Alzheimer's disease in particular, are less common in people with higher levels of education. For example in a Canadian study, people with more than ten years' education were four and a half times less likely to have dementia than those with less than six years' education.<sup>2</sup> However researchers are not yet certain of the reasons for this. For instance it is not known whether it is education which is important or other factors related to it like natural intelligence or family income. It may also be important to keep mentally active throughout life. One possibility is

that higher education may delay the onset of dementia. As with other factors affecting risk, it should be borne in mind that many people with a high level of education may still develop dementia later in life and that most people with lower levels of education will still not develop dementia.

**Stroke and vascular disease.** Dementia develops in approximately a third of people who survive to three months after a stroke.<sup>3</sup> The distinction between Alzheimer's disease and 'vascular dementia' is becoming less clear since many people who develop dementia after a stroke appear to develop Alzheimer's disease rather than a dementia which is explained by further strokes.<sup>4</sup> It is possible that the presence of small strokes may bring forward the age at which the symptoms of Alzheimer's disease are noticed.<sup>5</sup> People who have diseases which affect the circulation (such as high blood pressure, diabetes, and heart disease) have a higher than average risk of developing dementia – again apparently both vascular dementia and Alzheimer's disease.<sup>6</sup> It is likely that treatment of conditions which affect the circulation will reduce this risk,<sup>7</sup> although this is still being actively researched.

**Smoking.** This is still uncertain. People who smoke are known to have a higher than average risk of heart disease and stroke and some studies have suggested that they have a higher risk of dementia (approximately a two-fold increased risk in one study).<sup>8</sup> Early research findings had suggested that smoking might protect against Alzheimer's disease but this has not been confirmed by larger, more recent studies which have suggested that smoking, if anything, *increases* the risk of Alzheimer's disease.<sup>2</sup>

**Alcohol.** People who drink excessive amounts of alcohol over a prolonged period of time may develop dementia, in addition to many other health problems. This may be due to damaging effects of alcohol directly on the brain or by a lack of particular vitamins in people who drink heavily. The association between moderate levels of consumption and risk of dementia is still being researched: in particular whether a small amount of alcohol on a regular basis may be protective.

**Head injury.** People who take part in boxing are at risk of developing a particular type of dementia which is believed to be caused by repeated blows to the head. Some studies also found that head injury had occurred about two times more commonly than expected in people with Alzheimer's disease. Head injury in this context means any blow to the head causing loss of consciousness for at least

15 minutes. However, one large follow-up study has recently found that the risk of future dementia in people with previous head injury was no higher than expected.<sup>9</sup> It is therefore possible that previous findings were due to the differences in recall mentioned earlier.

**Anti-inflammatory medication and Hormone Replacement Therapy (HRT).** Several studies have suggested that people who take anti-inflammatory drugs for health conditions such as arthritis have a lower risk of developing Alzheimer's disease. In addition, some studies have suggested that women who take Hormone Replacement Therapy after the menopause are less likely to develop Alzheimer's disease. These drugs could possibly inhibit the progression of Alzheimer's disease processes but might also be acting to reduce the risk of added vascular damage to the brain. Research is currently in progress to establish whether these drugs may protect against dementia. In particular, definitive evidence is only likely to come from randomised controlled trials – the standard procedure for evaluating any potentially beneficial medicine.

**Depression.** Older people with depression (persistent low mood) have a two to three times higher risk than expected of developing dementia.<sup>10</sup> However it is not yet known whether depression is a risk factor or whether it is simply an early symptom of dementia.

**Other health conditions.** Dementia may be caused by some infections (such as syphilis and AIDS) or by deficiencies in certain vitamins (such as vitamin B12, folic acid or thiamine). Treatment of these problems may sometimes improve mental function. However it is very rarely the case that dementia in older age is caused by one of these problems. Dementia may occur as part of other diseases which affect the brain, such as Parkinson's disease, Huntington's disease, Creutzfeldt-Jakob disease (CJD) and multiple sclerosis (MS). Dementia may also occur in some severe physical diseases such as kidney or liver failure, severe chronic bronchitis, and advanced cancer.

While substantial progress has been made in identifying possible risk factors for dementia, there is a long way still to go. Many of the factors outlined above are still being intensively investigated. Research is also focussing on other less established factors such as the role of diet, physical exercise and environmental exposures. Wide geographical variations in rates of dementia have been suggested (see *Factsheet 3*) which may well provide further clues for risk factor research. In addition, it is likely that further genetic

factors will be identified over the next few years. How all these factors ultimately fit together in affecting risk for dementia will be a major question for future research.

1. van Duijn CM, Stijnen T, Hofman A. Risk factors for Alzheimer's disease: overview of the EURODEM collaborative re-analysis of case-control studies. *Int J Epidemiol* 1991;20(suppl 2):S1-S73
2. Canadian Study of Health and Aging. Risk factors for Alzheimer's disease in Canada. *Neurology* 1994;44:2073-2080.
3. Pohjasvaara T, Erkinjuntti T, Ylikoski R, Hietanen M, Vataja R, Kaste M. Clinical determinants of poststroke dementia. *Stroke* 1998;29:75-81.
4. Kokmen E, Whistman JP, O'Fallon WM, Chu CP, Beard CM. Dementia after ischemic stroke: a population-based study in Rochester, Minnesota (1960-1984). *Neurology* 1996;19:154-159.
5. Snowdon DA, Greiner LH, Mortimer JA, Riley KP, Greiner PA, Markesbery WR. Brain infarction and the clinical expression of Alzheimer disease. *JAMA* 1997;277:813-817.
6. Stewart R. Cardiovascular factors in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 1998;65:143-147.
7. Forette F, Seux M-L, Staessen JA, Thijs L, Birkenhager WH, Babarskiene M-R, et al. Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet* 1998;352:1347-1351.
8. Ott A, Slioter AJC, Hofman A, van Harskamp F, Witteman JCM, Van Broeckhoven C, et al. Smoking and the risk of dementia and Alzheimer's disease in a population-based cohort study: The Rotterdam Study. *Lancet* 1998;351:1840-1843.
9. Mehta KM, Ott A, Kalmijn S, Slioter AJC, van Duijn CM, Hofman A, et al. Head trauma and risk of dementia and Alzheimer's disease. *Neurology* 1999;53:1959-1962.
10. Devenand DP, Sano M, Tang MX, Taylor S, Gurland BJ, Wilder D, et al. Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. *Arch Gen Psychiatry* 1996;53:175-182.

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Dr Robert Stewart  
Clinical Research Fellow  
Section of Old Age Psychiatry  
Institute of Psychiatry  
London, UK  
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### Alzheimer's Disease International

For more information about Alzheimer's disease and Alzheimer's Disease International, contact:  
Alzheimer's Disease International  
45/46 Lower Marsh  
London SE1 7RG  
United Kingdom  
Tel: +44 20 7620 3011  
Fax: +44 20 7401 7351  
Email: [adi@alz.co.uk](mailto:adi@alz.co.uk)  
Web: [www.alz.co.uk](http://www.alz.co.uk)