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Update on Alzheimer's Disease. Alzheimer's disease (AD) is a chronic progressive neurodegenerative disorder. A recent paper reviewed the disease and its management (*BMJ 2009; 338: 467-71*). AD is characterised by 3 primary groups of symptoms: (1) cognitive dysfunction (memory loss, difficulties with language, high level skills) (2) non-cognitive symptoms (psychiatric symptoms and behavioural disturbances) and (3) difficulties with activities of daily living (basic skills e.g. eating / dressing and complex skills

e.g. driving). **Patients usually present with mild memory loss** (mild cognitive dysfunction) which may be stable for many years. Although the prognostic value of this for the development of AD is controversial, patients with mild cognitive dysfunction associated with memory loss have been shown to be 15 times more likely to develop AD than those without these symptoms. This phase is followed by a **detectable decline in cognitive function** (e.g. loss of memory resulting in impaired activities, apathy, forgetfulness), lasting 2-5 years. This is followed by **further decline in daily activities**, coupled with the appearance of behavioural and psychological symptoms of dementia (depression, anxiety, delusions). Continuing deterioration causes **progressive physical and mental disability** resulting in the patient becoming bedbound, with no basic psychomotor skills. This symptom progression may take up to 9 years in AD. **Diagnosis:** A history should be taken both from the patient and, ideally a knowledgeable informant. A mental state assessment should include a validated cognitive function test (the clock test may be useful in general practice as it is non-confrontational and the normal drawing of a clock more or less excludes the presence of important impairment). Other causes of dementia and depression (e.g. vascular and neurological) should be excluded. The **cause** of AD is unknown but the following are thought to be risk factors: family history, head injury, depression and vascular conditions such as hypertension, high cholesterol, atrial fibrillation. There is no consistent evidence of increased risk associated with dietary factors including aluminium, smoking or gender. Treatment consists of pharmacotherapy and environmental support. The cholinesterase inhibitors (**donepezil, rivastigmine, galantamine**) are authorised for the management of mild to moderately severe AD and **memantine** is authorised for moderate to severe AD. (It is recommended that these medicines are prescribed by experienced physicians). They have been shown to improve symptoms in a substantial minority of AD patients and are generally well-tolerated. Behavioural and psychological difficulties may also require medication but should only be prescribed under specialist advice; antipsychotic drugs may reduce agitation, however they have been linked with an increased risk of mortality and may impair cognition. **Non-drug therapies** are not effective in modifying memory loss but can alleviate the behavioural symptoms and improve patient well-being. These include environmental issues (ensuring continuity of care staff and privacy if possible, improvement in communication with care providers, encouraging daily activities including exercise) and therapies such as aromatherapy, multisensory stimulation, light therapy or music (which may be helpful for agitation). **It is important to rule out any physical cause (e.g pain) for a worsening of behaviour.** The authors conclude that multi-component intervention programmes give the best results for AD patients and their carers.



Do multivitamins prevent cancer and cardiovascular disease? An analysis of data from the Women's Health Initiative (WHI) study looked at the association between multivitamin (MV) use and the risk of specific solid tumours (breast, endometrial, lung, colorectal and ovarian cancer), cardiovascular disease (CVD) and mortality (*Arch Intern Med. 2009;16: 9294-304*). The study included 161,808 postmenopausal women who were followed up for a median duration of 8 years. The overall results found that 42% of women had used MV but **MV use was not associated with any significant reduction in risk of the cancers studied, CVD outcomes or total**

mortality. The authors conclude that the study suggests that MV use has little or no influence on the risk of cancer or CVD in postmenopausal women.



Should you administer medication through an enteral feeding tube?

The NMIC frequently receives queries about the administration of medication through enteral feeding tubes (usually outside the product authorisation). A review of this topic was recently published (*Am J Health-Syst Pharm* 2008; 65: 2347-57). Enteral nutrition (EN) through a feeding tube (FT) may be the preferred method of nutritional support in selected patients unable to feed orally. The FT may also be used for administering medications in those unable to swallow safely. Nasoenteric EN is commonly used for patients requiring short-term EN while percutaneous endoscopic gastrostomy is more commonly used for those requiring long-term EN. Several issues

should be considered when administering oral medications through a FT including: blocked FT, decreased drug effectiveness and increased adverse effects or drug-formula incompatibilities. **Dosage form** is an important factor to consider: **liquid formulations are preferred** when possible as they are readily absorbed and less likely to cause tube occlusions (elixirs or suspensions more favoured than syrups, which can occlude the FT). Liquid formulations can however be hypertonic (and may require dilution) or contain sorbitol (may increase the risk of GI intolerance) and some liquid formulations are not appropriate for administration through a FT (e.g. metronidazole suspension). **Certain dosage forms are not suitable for crushing and administering through a FT** including **enteric-coated products, some extended release products and medications with carcinogenic, teratogenic or cytotoxic properties**. Other solid dosage forms can be crushed when liquid formulations are not available, about which advice should be sought. The addition of medication directly to enteral formula should be avoided as it can result in physical incompatibilities, risk of occlusion and potential microbial contamination. Medications should be given as a bolus separate from EN feeding with tubes flushed with up to 30 ml water before and after medication administration. There are specific **drug-food interactions** which have been reported including those involving: phenytoin, carbamazepine, fluoroquinolones and proton pump inhibitors, resulting in reduced absorption of the drug, and there have also been reports of warfarin resistance in those receiving EN. Patients should be continuously monitored for the appropriate clinical response to their medications and it is recommended that guidelines should be established for the effective delivery of medications via this route. [Editors note: the NMIC can provide help with queries of this nature].



Fertility drugs and risk of ovarian cancer. Nulliparous women have a higher risk of ovarian cancer than parous women, however concerns have been raised of an association between infertility and/or use of fertility drugs and ovarian cancer. A recent study assessed the effects of fertility drugs on the overall risk of ovarian cancer in a cohort of women (n=54,362) attending Danish infertility clinics (*BMJ* 2009;338:249 doi:10.1136/bmj.b249). The median age at first evaluation of infertility was 30 years and the end of follow-up was 47 years. Women (n=156) diagnosed with invasive epithelial ovarian cancer were compared with 1241 women randomly selected from the cohort (=control group).

The main outcome was the effect of fertility drugs (gonadotrophins, clomiphene, human chorionic gonadotrophin or gonadotrophin releasing hormone) on overall risk of ovarian cancer. Adjustment for potential confounding factors (including parity and maternal age at birth of first child) was made. Fertility drugs had been used by 49% of the ovarian cancer group and 50% of the control group. The results showed the **overall risk of ovarian cancer was not significantly affected by use of any fertility drug**. There was also no difference in overall risk for the number of cycles of use, length of follow-up since first use or parity. A major limitation was that the median age at follow-up was 47 years, which is below the peak age for ovarian cancer (early 60's). The authors conclude that the study showed no strong association between the use of fertility drugs, however further follow-up is needed.