Table 1

Causes of young onset dementia adapted from Sampson et al. *Postgrad Med J* 2004; 80:125-139[3]

Disease	Clinical features
Primary neurodegeneration	
Alzheimer's disease	
● Amnestic Alzheimer's disease	Episodic and topographical memory impairment
● Posterior cortical atrophy	Visuospatial and visuoperceptual impairment
● Logopenic variant primary progressive aphasia	Word finding pauses, slow speech rate, poor sentence repetition
Frontotemporal dementias	
● Behavioural variant frontotemporal dementia	Behavioural change, apathy
● Semantic variant primary progressive aphasia	Semantic impairment, word finding, surface dyslexia
● Non-fluent primary progressive aphasia	Phonologically and grammatically distorted speech
● Corticobasal degeneration	Limb apraxia, asymmetric parkinsonism
● Progressive supranuclear palsy	Falls, ophthalmoplegia, axial rigidity, frontal syndrome
● Frontotemporal dementia with motor neurone disease	Apathy, disinhibition, weakness and wasting of limb muscles
Dementia with Lewy bodies	Visuospatial and executive impairment, fluctuating impairment, visual hallucinations
Multiple system atrophy	Parkinsonian features, cerebellar ataxia, autonomic dysfunction, poor attention and executive function
Parkinson's disease	Dysexecutive syndrome, bradyphrenia (slowing of thought)
Huntington's disease	Personality change, adventitious movements, poor memory, attention and executive function
Vascular	
Strategic infarct	Rapid onset severe cognitive impairment, fluctuating cognitive function
Multiple cortical infarcts	Urinary and gait disturbance, features of pseudobulbar palsy, fluctuating cognitive function
Small vessel disease	History of hypertension/diabetes mellitus, poor executive function and processing speed
CADASIL	Psychiatric disturbance, migraine, strokes
Cerebral amyloid angiopathies	Episodes of confusion, delirium, impaired vision, speech impairment, seizures
Fabry's disease	Small vessel disease, renal disease, skin changes, pain in extremities
Prion	
Creutzfeldt-Jakob disease	Memory loss, personality change, hallucinations, florid myoclonus, ataxia, mood disorder
Inflammatory	
Multiple sclerosis	Frontal subcortical syndrome, absent abdominal reflexes
Vasculitis associated with systemic disorders	Headaches, fluctuating symptoms, seizures, rapid deterioration
Primary angiitis of central nervous system	Behavioural changes, ataxia, fluctuating symptoms, seizures, rapid deterioration
Neurosarcoidosis	Excessive fatigue, excessive thirst, confusion, delirium, speech impairment
Behcet's disease	Genital ulcers, skin lesions, eye inflammation
Neoplastic/paraneoplastic	
Tumours	Raised intracranial pressure, frontal dysexecutive syndrome
Limbic encephalitis	Weight loss, hallucinations, seizures, short-term memory loss, psychiatric symptoms
Infections	
Tuberculosis meningitis	Risk factors, memory loss, incoherence
HIV/AIDS dementia complex	Impaired memory and concentration, motor deficits, apathy
Whipple's disease	Gastrointestinal symptoms, visual impairment, memory loss, confusion
Lyme disease	Suspicion of tick bite, psychiatric symptoms, memory loss, poor attention
Neurosyphilis	Multiple strokes, tremor, seizures, poor memory, mood disturbance
Subacute slerosing panencephalitis	Florid myoclonus and seizures, rapid deterioration
Progressive multifocal leukoencephalopathy	Posterior cortical syndrome
Metabolic	
Endocrinopathies	Variable cognitive features depending upon underlying condition
Nutritional deficiencies	Variable cognitive features depending upon underlying deficiency
Uraemia	Fluctuating attention/arousal, personality change, cognitive impairment, asterixis, renal failure
Hepatic encephalopathy	Fluctuating attention/arousal, personality change, cognitive impairment, asterixis, hepatic failure
Wilson's disease	Dysarthria, poor coordination, parkinsonian features, poor attention and memory, apathy, disinhibition

Table 1 *continued*

Causes of young onset dementia

Disease	Clinical features
Toxins	
Alcohol	Impaired executive function and autobiographical memory, confabulation, Wernicke-Korsakoff syndrome
Carbon monoxide/lead/prescription drugs	Suspicion of exposure
Epilepsy	Discrete episodes, temporary confusion, poor/patchy memory and attention, cognitive slowing
Other	
Post irradiation	History of cranial irradiation, ataxia, seizures
Obstructive sleep apnoea	Obesity, morning headaches, excessive snoring
Chronic subdural haematoma	History of head trauma, frontal subcortical syndrome
Hydrocephalus	History of meningitis, gait apraxia, urinary incontinence
Dementia pugilistica	History of repeated head injury/trauma, parkinsonism

For more detailed information see Rosser et al *Lancet Neurol* 2010;9:793-806 and Masellis et al. *Alzheimer's Res Ther* 2013;5(S1):S7

cognitive symptoms in order to identify which patients need referral to specialist centres, and which can be reassured and spared extensive and costly investigations.

COMMON CAUSES

The list of causes of YOD is extensive, see table 1, left and above. Epidemiological studies conducted in the UK have found that the most common causes of YOD are early onset forms of adult neurodegenerative conditions and alcohol, see table 2, below.[4]

Table 2

Common causes of young onset dementia

Alzheimer's disease	30%
Vascular dementia	15%
Frontotemporal dementia	13%
Dementia with Lewy Bodies	4%
Alcohol-related dementia	12%
Other	25%

Alzheimer's disease

Alzheimer's disease (AD) is defined by histopathology: extracellular plaques of beta-amyloid protein and intracellular tangles of hyperphosphorylated protein tau. The clinical phenotype of young onset AD is heterogeneous. In a proportion of AD patients, the presenting features deviate from the classic memory presentation, and include salient visuospatial or language impairment. Autosomal dominant AD is more common among YOD, but still only represents < 1% of all AD cases.[5] The presence of mutations in three genes has been identified: amyloid precursor protein (APP), presenilin 1 (PS1) and presenilin 2 (PS2). Carriers can develop AD as early as their 30s. Evidence also suggests that people with Down's syndrome have an increased risk of developing early onset AD due to the overexpression of the APP gene.

Amnestic Alzheimer's disease (amAD): The large majority of cases present with classic symptoms of memory decline, including forgetfulness relating to daily tasks and events (episodic memory impairment) and disorientation in familiar environments (topographical memory impairment), reflecting pathology in the medial temporal lobe. Other early signs may include word finding difficulty, apraxia[6] and visuospatial errors.

Posterior cortical atrophy (PCA): Patients with PCA present with core visuospatial and visuoperceptual impairment not explained by ocular disease but rather by higher visual processing deficits. Brain imaging reveals predominant posterior (occipito-parietal) cortical atrophy. Typical features are simultanagnosia (an inability to discern individual objects in a cluttered visual environment), visual neglect, and difficulty judging visual distance or movement. Limb apraxia is a common accompaniment. Recent evidence suggests memory impairment can also be an early feature.[7]

Logopenic primary progressive aphasia (lvPPA): In this AD variant, the predominant problem is with language function rather than memory. Speech output in lvPPA is characterised by a slow production rate, long word finding pauses and difficulty with sentence (but not single word) repetition. Imaging reveals atrophy of the left temporoparietal gyri.[8]

Vascular dementia

Vascular dementia (VaD) is the second most common cause of YOD after AD. Conventional vascular risk factors may be absent and diagnosis relies on imaging evidence of cerebrovascular disease. In younger people with YOD, atypical haematological, metabolic or genetic causes should be considered, such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and cerebral amyloid angiopathy (CAA).[9]

The term VaD comprises several heterogeneous syndromes:

- Multiple cortical infarcts are commonly characterised by early urinary and gait disturbance and features of pseudobulbar palsy. A background of thromboembolic disease is also common
- Strategic infarcts produce rapid onset cognitive impairment. Patients do not often have classical focal neurological signs
- Small vessel disease is frequently associated with hypertension and diabetes mellitus. Patients perform poorly on tests of executive function and processing speed. Fluctuations in cognitive function and emotional lability are commonly observed.

Frontotemporal dementias

The frontotemporal dementias (FTD) form a spectrum of neurodegenerative disorders which can be broadly clustered into three groups — behavioural, language and motor »