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Mental Changes in Parkinsonism

James Parkinson's elegant and detailed description[1] of six patients who displayed "involuntary tremulous motion, with lessened muscular power, in parts not in action and even when unsupported: with a propensity to bend the trunk forward, and to pass from walking to a running pace" added that the senses and intellect were unaffected. Since then evidence has accumulated that there is an increased prevalence of dementia in Parkinsonism.[2] This dementia cannot always be attributed to concomitant cerebrovascular disease, for though atherosclerosis is common in the Parkinsonian age group in general there is a poor correlation between the two conditions.[3] Many now consider that "arteriosclerotic Parkinsonism" has no firm pathological basis,[4] in which case the dementia may be due to cerebral atrophy consequent upon the same degenerative process as that responsible for the nigrostriatal lesions of idiopathic Parkinsonism.

Other mental changes are often encountered in Parkinsonism. Depression is frequently out of proportion to the neurological deficit.[5] Confusion, delusions, and hallucinations occur—though they are usually caused by the anticholinergic drugs employed as therapeutic agents. Estimates[6 7] of the prevalence of such symptoms induced by anticholinergic drugs range from 19 to 30%. Stereotactic surgery may contribute to some of the psychiatric features of Parkinsonism, but a careful study of intellectual impairment by Loranger *et al.*[8] concluded that these features could not all be explained by "the additive effects of depression, peripheral motor disability, anticholinergic drugs, and thalamotomy or pallidectomy." This conclusion was in agreement with Ball's comment,[9] almost a century ago, "I would willingly say that a slight degree of intellectual disturbance is almost the rule in this disease."

With this background recent reports attributing mental changes to treatment with levodopa must be evaluated with caution. In a comprehensive review of adverse reactions to levodopa Barbeau *et al.* estimated[10] that 10 to 25% of patients on long-term therapy develop psychiatric symptoms; in postencephalitic patients the proportion is higher.[11] The common problems are agitation, irritability, and insomnia, which may progress to impaired judgement, anger, and hostility. Occasionally anxiety, fear, and apprehension acquire paranoid features or progress into hypomania. Somnolence has also been reported.[12] Bizarre, stereotyped, and often obsessional behaviour can occur, and hallucinations may be present. Loss of inhibition probably contributes to some of the reports of increased sexual activity, though it is likely that a general improvement in mobility consequent upon the therapeutic action of levodopa plays an equally significant role. Some patients are reported to have become depressed, and there have been a few cases of attempted suicide. The outstanding common denominator of this long list of disturbing adverse reactions is that all clear on stopping levodopa, though occasionally this may take several weeks.[10]

In contrast to these reversible manifestations of toxicity rare cases of sustained mental deterioration have been reported, though their relationship to levodopa therapy remains unproved. In one patient[12] confusion and hallucinations progressed to epilepsy and stupor which lasted several weeks after stopping levodopa. Consciousness was then regained, though the patient remained confined to bed. Pneumoencephalography showed generalized cerebral atrophy, but large cerebral ventricles had been recorded 10 years earlier when the patient had undergone bilateral stereotactic surgery. In a more recent report[13] a patient receiving benzhexol, amantadine, and levodopa developed confusion and hallucinations, so all drugs were stopped. He progressed to stupor, which lasted eight days. When he regained consciousness he was profoundly demented and remained so until his death four months later. Necropsy showed cerebral atrophy and the neuropathological features of idiopathic Parkinsonism, and there was mild cerebral atherosclerosis with a few small cerebellar infarcts. There was no postmortem explanation for his acute deterioration.

It is not possible to draw any firm conclusion when many thousands of Parkinsonian patients have now been receiving substantial doses of levodopa for several years and the reports of irreversible mental deterioration are so limited. However, accounts of stupor and dementia should alert physicians to continue careful surveillance of all patients on long-term therapy with levodopa. It is only by notification of all unexpected findings to the Committee on Safety of Medicines that sufficient experience can be built up for a causal relationship to be established or refuted.

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Gastroenteritis from Cheese

Even those with palates for very ripe cheese do not apparently risk their health in eating it. The occasional illness such as brucellosis from cheese[1 2] is usually traced to some brought privately from abroad and not to cheese sold commercially in Britain. Reports[3] from the U.S.A. of a widespread outbreak of gastroenteritis in adults due to imported cheese are therefore of some interest not only because of the food concerned but also because the offending organism, an enteropathogenic strain of *Escherichia coli*, is usually associated with illness in infants.

The outbreak[4] was known to have affected at least 387 of 409 persons at risk (95%) in 13 states in the space of four weeks at the end of 1971. Many of those affected developed a dysentery-like syndrome, associated in a few with the passage of blood. Six patients required hospital admission, but no deaths are known to have occurred.

From epidemiological investigations camembert and brie cheeses imported from France were strongly suspected to be the source of the outbreak; this was confirmed when *E. coli* 0124: B17 was isolated from the stools of several patients and from samples of the implicated cheeses. The same serotype was also isolated from a sample of coulommiers cheese produced by another factory in France but imported into the U.S.A. by the same firm, though no documented cases of gastroenteritis were attributed to that cheese. All the cheeses that had already been distributed were recalled by the importers. The recall was monitored by the U.S. Food and Drug Administration, and no further cases of gastroenteritis from French cheese have been reported since.

Though three brands of brie and camembert cheeses were implicated they had all been imported by one firm in New York and had been produced in one factory in France—and indeed were identical except for their shapes.[3] All the cheese had been manufactured during two days, and *E. coli* 0124 was isolated in the factory from the curdling tank and from samples of cheese. The probable source of infection was river water used in cleaning equipment: the filtration system at the factory had not been working efficiently at the time.[5] Further details of the treatment of river water for use in the factory were not available, but a filtration system alone is commonly regarded as insufficient to guarantee the purity of water for use in food manufacturing premises—chlorination is usually required. Fine filters capable of removing bacteria and even viruses from water are available, but these are impracticable with the large volumes required in manufacturing processes, especially with river water as a source. A coarse filter was most probably used, and this would remove large particles and organisms such as algae only. Hyperchlorination of the filtered water would then be necessary followed by dechlorination using a carbon filter.

Gastroenteritis in infants from enteropathogenic serotypes of *E. coli* is well recognized, and outbreaks are commonly reported,[6-8] and symptoms may also be produced in volunteer adults and children.[9-13] Reports of outbreaks in adults are, however, few. In 1949 Hobbs, Thomas, and Taylor[14] described a school outbreak of gastroenteritis associated with a pathogenic paracolon bacillus (now known as *E. coli* 0124) and were able to reproduce symptoms in volunteer experiments. A year later Stevenson[15] reported the occurrence of *E. coli* D433 (*E. coli* 0111) in the stools of adult patients with diarrhoea. More recently, in an investigation of travellers' diarrhoea in a group of British soldiers in Aden[16] a new *E. coli* serotype, 0148, was found in as many as 54% of those who had diarrhoea but not in any of those without diarrhoea. Last year 87 of 714 adults developed diarrhoea less than 24 hours after eating ham and egg pie,[17] and *E. coli* 0127 was isolated from all 15 patients investigated and from samples of pie remains and unused pies. It seems probable that outbreaks of *E. coli* gastroenteritis in adults may be more common than hitherto recognized.

The cheese associated with the outbreak in the U.S.A. was stated to have been consumed in France and the U.S.A. only, though there were no reports of gastroenteritis from this source in France. There have also been no reports to date of gastroenteritis from French cheese in Britain and, indeed, the moral to be drawn from this outbreak is not to beware of French cheese. The real lessons are much broader. Firstly, in the investigation of an outbreak of foodborne gastroenteritis the bacteriologist's search must not be considered to be complete if salmonellas, *Staphylococcus aureus*, and *Clostridium welchii* are not identified. In recent years, *Vibrio parahaemolyticus*,[18 19] non-agglutinating vibrios,[20] (*Bacillus cereus*,[21 22] and now *E. coli* have also been incriminated in outbreaks of food-poisoning and must be looked for in appropriate instances. Secondly, it is important not to assume that a particular food is innocent because it has never been known to cause gastroenteritis.

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Cars or Chairs?

For some time pressure has been mounting to replace three-wheeler invalid cars by specially converted conventional motor cars. Last week there appeared a critical examination by Baroness Sharp of the consequences of such a change.[1]

Lady Sharp's report was prepared without knowledge of any official verdict on the safety of three-wheelers; but, as