

SYMPOSIUM

TREATMENT OF PARKINSON'S DISEASE

The following paper's were given at the above symposium held at Glasgow Royal Infirmary on 4 December 1985. The symposium was chaired by Dr C.D. Forbes. The symposium and the publication of the papers has been generously supported by Roche Products Ltd.

THE DRUG TREATMENT OF PARKINSONISM

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PARKINSONISM, perhaps the most easily recognisable neurological disease, remains unconquered. Neuronal degeneration in the substantia nigra was associated with a critical deficiency of the neurotransmitter dopamine and 20 years ago levodopa was introduced as a logical form of replacement therapy. This triggered a remarkable expansion in our knowledge of the neuro-chemistry of the basal ganglia. This form of treatment and the prolonged survival of the patients have been complicated by an array of symptoms which have proved difficult to control. Thus the complete relief of Parkinsonism remains an elusive ideal and it continues to stimulate constructive thought about normal and disordered cerebral function.

Parkinsonism is characterised by tremor, rigidity and bradykinesia. Bradykinesia is a term which encompasses an inability to generate those relaxed patterns of muscular activity and posture upon which precise and consciously directed movements are superimposed. From an analogy with computers one might think in terms of programmes for particular movements, but it seems unlikely that the programmes could be stored in the basal ganglia. It is more probable that the programmed material is in the accessory motor cortex or parietal cortex and that it is activated by the basal ganglia under the influence of afferent impulses mediated by the cerebellum.

Fifteen to twenty neurotransmitters have been recognised as having specific receptor sites in the basal ganglia (1). Dopamine and some, perhaps all, of the other neurotrans-

mitters have agonist and antagonist properties at the same site under different physiological conditions. One site may have more than one type of receptor for a single transmitter, again clearly demonstrated in the case of dopamine (2). In the light of this there should be no surprise about some of the bizarre and paradoxical effects of the drugs which we use.

Recognising the potential complexity of the situation let us return to the perhaps oversimplified basic deficiency of Parkinsonism, namely that of dopamine in the nigrostriatal system; in turn disturbing the notional balance between dopaminergic and cholinergic activity. The availability of levodopa particularly in combination with the extracerebral decarboxylase inhibitors provides replacement therapy and spectacular relief of symptoms. In idiopathic Parkinsonism it is almost universally effective with relatively little in the way of unacceptable side effects when first used. High blood levels of dopa presumably paralleling the high levels of dopa-dopamine in the brain are associated with an overflow of involuntary movements termed dyskinesia even in the earliest days of treatment. They usually equate with the maximal relief of bradykinetic symptoms and the dosage can be adjusted to keep an acceptable balance between the relief of symptoms and dyskinesia.

With prolonged treatment the benefits are lost. After five to ten years not only have the presenting symptoms returned with increased severity but new disabilities have developed. The period of effectiveness of an individual dose becomes shorter. The

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Parkinsonism: Physiology, Pharmacology and Treatment Donald Brian Calne, 1970 *Parkinsonism* Donald B. Calne, O. Hornykiewicz, 1970 Psychopharmacology Abstracts, 1970 **Progress in the Treatment of Parkinsonism** Donald Brian Calne, 1973 **Catecholamines** Hermann Blaschko, Erich Muscholl, 2012-12-06 Catecholamines 1922 1971 H BLASCHKO Adrenaline and related substances were discussed in the 1924 edition of Hefl ter s Handbook by PAUL TRENDELENBURG On 164 pages he described what was then known not only of adrenaline and its closest relatives but also of the sympathomimetic compounds such as tyramine and ephedrine When the present Editors of the Handbook entrusted us with the task of editing the present Volume it was decided to restrict it to adrenaline and the other naturally occurring catecholamines The sympathomimetic amines in general will be discussed only in their relation to the catecholamines Since TRENDELENBURG completed his review this field has undergone an enormous expansion There has been a wealth of new findings and a succession of new ideas The new theories that have been built into contemporary thought will be fully discussed in the succeeding contributions But many of the hypotheses that have been put forward since 1924 have long been discarded and yet they have often led to important observations that we still consider as valid **Functional and Stereotactic Neurosurgery** E.I. Kandel, 2012-12-06 Soon after neurosurgery had advanced past the stage of that older neurosurgeons will consider their cra removing lesions on the surface of the brain it became niotomies quite adequate for the relief of many neu apparent that subcortical diseased tissue could not be rological disorders that Professor Kandel shows so excised safely by the usual surgical techniques because clearly to be amenable to stereotactic intervention of the risk of damaging overlying normal structures there are many lesions that undoubtedly can be reached Various means of reaching deep seated lesions were more easily and with less risk to life and limb by ster devised most of which attempted to approach the eotactic than by open procedures pathological tissue through silent areas of the brain This book is not just a description of operative However these operations often resulted in serious procedures although it does give clear accounts of neurological deficits Spiegel and Wycis s modifica surgical techniques It presents the postoperative histo tion of the Horsley Clarke apparatus to reach targets ries of patients who have been cured or markedly re deep in the human brain introduced a new approach to lieved of longstanding afflictions these persons have subcortical surgery True as Professor Edward Kandel been followed for 10 to 15 or more years so that the relates Russian surgeons had pioneered in the field results may be considered more or less permanent **Current Catalog** National Library of Medicine (U.S.), 1979 First multi year cumulation covers six years 1965 70 Advances in Parkinsonism Walther Birkmayer, Oleh Hornykiewicz, 1976 **Dopaminergic Ergot Derivatives and Motor Function** Kjell Fuxe, Donald B. Calne, 2013-10-22 Dopaminergic Ergot Derivatives and Motor Function is a collection of papers from the proceedings of an international symposium of the same topic held in Stockholm on July 24 25 1978 This collection of papers covers laboratory studies on different subjects such as

the anatomy physiology biochemistry and pharmacology of dopaminergic pathways of the brain This book also discusses clinical research dealing on dopaminergic receptors observed in Parkinsonism and in Huntington s disease One paper reviews the neural circuitry of the basal ganglia as it is the part of the brain that is first and foremost involved in skeletomuscular mechanisms Another paper deals with the different groups of ergot derivatives and their structure activity relationships The book also addresses the therapeutic activity and toxicity made during these observations The text then discusses the psychiatric reaction to ergot derivatives including LSD induced hallucinations Another paper examines the effects of dopaminergic ergots on the anterior pituitary function that is limited to the control of prolactin secretion during chronic therapy This book is valuable to microbiologists microchemists and laboratory researchers and scientists dealing with neuro functions and the brain **National Library of Medicine Current Catalog** National Library of Medicine (U.S.),1971 First multi year cumulation covers six years 1965 70

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