11 *The classification of Parkinson's disease*

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11.1 INTRODUCTION: CURRENT CLASSIFICATION

The nosological classification of the syndrome of akinesia, rigidity and tremor with disturbances of posture and postural reflexes has been a matter of debate since its central features were first described under the heading of 'paralysis agitans' by James Parkinson in 1817. This designation was later criticized by Charcot (1880) on the grounds that muscular weakness is not part of the syndrome and tremor is not invariable but it was mainly Charcot's influence that led to common use of the term Parkinson's disease in preference to paralysis agitans. However, the nosological homogeneity of the disorder was increasingly questioned when the malady appeared to be the consequences of several possible pathological conditions of which cerebral arteriosclerosis was thought to be of particular importance in the early years of this century (Foerster, 1909, 1921; Souques, 1921; Jakob, 1923; Critchley, 1929). Lewy (1913) stated that the question of paralysis agitans was one of a particular localization of different pathological processes within the brain, and Souques (1921) taking the same view some years later wrote 'paralysis agitans or Parkinson's disease is not in my opinion a disease entity'. Now that damage to the dopaminergic nigrostriatal pathway has been recognized as the principal pathological event in causing the parkinsonian syndrome such statements remain valid for what it best termed 'secondary parkinsonism', that is, a motor syndrome due to an identifiable cause of damage to the nigrostriatal system. For the majority of cases however, a cause is not apparent and the syndrome does not only seem to be a matter of 'specific localization'. Assuming that there is homogeneity of the underlying mechanisms such cases continue to be classified as idiopathic Parkinson's disease. The neuronal inclusion bodies described by Lewy (1913) in the brains of Parkinsonian patients seem to be the most important pathological marker to support the nosological identity of idiopathic disease, not only from secondary

parkinsonism but also from a variety of cryptogenic diseases in which a parkinsonian syndrome forms part of the clinical picture. Based on such distinctions parkinsonian syndromes may be classified into three categories (Table 11.1).

Table 11.1 Classification of parkinsonian syndromes

(1)	Idiopathic Parkinson's Disease
(2)	Secondary (symptomatic) parkinsonism
(3)	Parkinsonism in multiple system degenerations

11.1.1 Secondary parkinsonism

In all the conditions listed in Table 11.2 a cause of nigrostriatal dysfunction can be identified and most are rare compared with the idiopathic disease (Chapter 15). Drug-induced parkinsonism following the administration of neuroleptic agents is the most frequent type in this group with a reported incidence of 7% in a recent epidemiological study (Rajput *et al.*, 1984). It has taken the place of post-encephalitic parkinsonism which used to be the most common secondary type in the first half of this century following epidemic outbreaks of encephalitis lethargica between 1917 and 1927 (Chapter 14), but no new cases were encountered between 1967 and 1979 in the study by Rajput and colleagues (1984). Parkinsonism following encephalitis lethargica is the most distinct type of secondary disease both clinically and pathologically, for which reason

Table 11.2 Classification of secondary parkinsonism

(1)	Post-encephalitic
	Drug-induced
	Toxic
	(a) exogenous, e.g. manganese, carbon monoxide, MPTP
	(b) endogenous, e.g. Wilson's disease
	Traumatic
	Neoplastic
(2)	Pseudo-parkinsonism
	Arteriosclerotic
	Normal pressure hydrocephalus

it has frequently been independently classified. In view of the fact that it is a manifestation of an identifiable pathological process and that it may be a sequel to other types of encephalitis (Duvoisin and Yahr, 1965), this does not seem to be necessary. Other forms of secondary parkinsonism listed in Table 11.2 are rarities but of considerable theoretical interest. This is especially the case with toxic parkinsonism caused by the meperidine analogue, MPTP, which has been recognized only recently and is particularly significant because of the selectivity of nigral damage produced and the species-specific toxicity (Williams, 1984). Arteriosclerotic parkinsonism which in the past was classified as the third major cause after the idiopathic and post-encephalitic forms (Critchley, 1929; Mjönes, 1949; Pollock and Hornabrook, 1966) is no longer widely accepted as a distinct type. The clinical picture of cerebral arteriosclerosis may well include signs such as bradykinesia and rigidity but other focal manifestations such as pyramidal, bulbar and cerebellar deficits with dementia are usually present; response to levodopa is absent or poor and there is no convincing evidence that the nigrostriatal pathway is actually involved in these conditions. For these reasons the term 'pseudo-parkinsonism' may be more appropriate for such cases (Critchley, 1983). They must not be confused, however, with idiopathic disease in which there is concomitant cerebral arteriosclerosis which seems to occur in parkinsonians with a frequency similar to that in the general population (Eadie and Sutherland, 1964). Parkinsonian syndromes seen in normal pressure hydrocephalus may be referred to as pseudo-parkinsonism for the same reasons.

11.1.2 Multiple system atrophies

Parkinsonism may be the clinical manifestation of a variety of conditions with comparably obscure aetiologies as idiopathic Parkinson's disease but with a more widespread degenerative pathology which affects other areas of the brain besides the substantia nigra. Parkinsonian multiple-system degenerations are listed in Table 11.3 in an order of frequency of occurrence in which they might initially simulate the idiopathic disease. Thus striatonigral degeneration is frequently misdiagnosed as idiopathic Parkinson's disease during life. Its distinguishing clinical features are unreliable and include akinetic-rigid manifestations, poor or absent response to levodopa treatment and rapid progression (Adams, 1968). Similar diagnostic difficulties exist with pallidonigral degeneration, the first cases of which were probably described by Hunt (1917) as juvenile paralysis agitans. Shy-Drager syndrome is easier to delineate clinically when autonomic failure becomes evident although dysautonomia may also be a feature of the idiopathic variety. Again, parkinsonian

symptoms in this condition usually respond poorly to levodopa therapy. The other entities listed in Table 11.3 are less likely to be clinically be mistaken for Parkinson's disease but nevertheless in one series 4% of cases diagnosed as idiopathic Parkinson's disease were found to have progressive supranuclear palsy (Jackson *et al.*, 1983). As more reports of the parkinsonism-dementia complex occurring outside the Western Pacific are published (Schmitt *et al.*, 1984) there is an increasing possibility of confusion with idiopathic Parkinson's disease.

Table 11.3 Parkinsonism in multi-system degenerations

Striatonigral degeneration
Pallidonigral degeneration
Shy-Drager syndrome (Multiple system atrophy with autonomic failure)
Olivo-ponto-cerebellar atrophy
Jakob-Creutzfeld disease
Hallervorden-Spatz disease
Rigid Huntington's disease

There is clearly a certain degree of overlap between idiopathic disease and some of the so-called parkinsonian multiple-system atrophies (Ropper, 1983). This applies not only to clinical features, but also to some of the pathological aspects since Lewy bodies have been found in cases of Shy-Drager syndrome (Vanderhaegen *et al.*, 1970; Langston and Forno, 1978). The question arises whether such zones of overlap become better defined by subdividing idiopathic Parkinson's disease into distinct subtypes.

11.2 ARE THERE CLINICALLY IDENTIFIABLE SUBGROUPS?

The cardinal symptoms of idiopathic Parkinson's disease usually show considerable variability of expression among different patients and terms like 'paralysis agitans sine agitatione' or 'paralysis agitans sine rigiditate' were employed by early observers (Souques, 1921; Foerster 1921; Lewy, 1923) to delineate predominantly rigid or tremulous forms of the disease which were sometimes regarded as 'formes frustes'. Such variability in clinical presentation of Parkinson's disease becomes even greater when cognitive symptoms or dysautonomia are considered; these may be prominent in some cases and absent in others. The onset is after age 60 and 70 years in the majority of cases but 'juvenile Parkinson's disease' with onset below the age of 40 years is not

infrequently observed. Rates of progression of the disease may vary between the extremes of patients remaining essentially stationary for decades or progressing to severe disability over a few years. Similarly the degree and type of response to levodopa may vary considerably among patients. Finally, despite the results of a twin study of Parkinson's disease showing a monozygotic concordance rate of only 4.7% (Ward *et al.*, 1983; Duvoisin, 1984) there are still claims for the existence of familial forms of idiopathic Parkinson's disease (Barbeau and Roy, 1984). But do such clinical variations form the basis for a significant subdivision into various types? Such a classification might lead to a clearer separation of patient groups in studies of the epidemiology and natural history of the disease and may also assist in the assessment of therapeutic trials. Perhaps more importantly it could provide a better basis for clinico-pathological correlations, especially in view of the opinions that there exist different pathological patterns in idiopathic Parkinson's disease (Forno and Ellsworth, 1971; Alvord *et al.*, 1975; and Chapter 6).

11.2.1 Juvenile disease

Age specific rates of prevalence and incidence of Parkinson's disease consistently show a peak after age 60 and 70 years in several epidemiological studies (Kessler, 1970; Kurland, 1958; Marttila and Rinne, 1976a; Rajput *et al.*, 1984). However, onset of the disease at ages below 40 years has long been recognized. Krafft-Ebing in 1898 reported 27–30 years to be the earliest age of onset in his series of patients and cites a report by Huchard in 1875 on a case of Parkinson's disease starting with tremor at the age of 3. In a review of the literature up to 1911 Willige found 46 cases of juvenile Parkinson's disease most of which he rejected as probably representing other diagnoses. In the cases he accepted as true examples of the disease the lowest age of onset was between 18 and 20 years and the secondary cases were present in about 50% of relatives. This author believed in the nosological independence of this type of Parkinson's disease and suggested the term 'paralysis agitans juvenilis familiaris' although he stated that there was no other major clinical difference between the juvenile and pre-senile cases. This view was also taken by Mjönes (1949) who furthermore, did not accept an independent nosological position for juvenile paralysis agitans. In more recent accounts of this condition a familial component is usually confirmed (Martin *et al.*, 1971; Yamamura *et al.*, 1973; Sachdev *et al.*, 1977; Yokochi and Narabayashi, 1981). Quinn *et al.* (1987) found this to be so only in a subgroup with onset of disease below the age of 21 years, while there was increased familial incidence in patients with onset of symptoms between 21 and 40 years, which they called 'young onset Parkinson's

disease'. In some reports the clinical presentation of juvenile Parkinson's disease is an akineto-rigid syndrome with little or no tremor. Barbeau and Pourcher (1982) however, describes a 'tremor-onset' form in addition to the akinetic-rigid type of juvenile Parkinson's disease and sporadic cases have shown the full range of symptoms seen in the classical disease (Clough *et al.*, 1981). The levodopa response is frequently characterized by the development of severe on–off fluctuations and dyskinesias (Yokochi and Narabayashi, 1981; Fischer, 1984). It is noteworthy that the latter was reported to be correlated with a younger age of onset in a study of levodopa long-term effects (Lesser *et al.*, 1979). The rate of progression is claimed to be slower in this variety than in the classical disease (Yokochi and Narabayashi, 1981; Scott and Brody, 1971).

There are no firm clinico-pathological correlations established for juvenile Parkinson's disease. Hunt (1917) describes striatal, especially pallidal, degeneration without nigral involvement in one of his 4 clinically typical cases of juvenile paralysis agitans, while Davison (1954) found the substantia nigra to be involved in a third of Hunt's original cases. Stadlan and co-workers (1965) detected Lewy bodies in the brain stem of only one of their 3 juvenile cases but in all of their 21 patients with pre-senile disease. While there is some evidence that juvenile paralysis agitans with onset before the age of 21 years might be a distinctive type of Parkinson's disease with a possible genetic basis, young-onset cases beginning between 21 and 40 years probably represent the lower end of the age distribution of idiopathic Lewy-body Parkinson's disease (Quinn *et al.*, 1987).

11.2.2 Variations in disease progression and response to levodopa

The observed rates of progression in Parkinson's disease prior to the use of leodopa vary considerably. Mjönes (1949) found 51% of 192 patients with paralysis agitans to be significantly disabled after up to 4 years, while in the series of Hoehn and Yahr (1967), where stricter criteria for severe disability were used, 25% of 271 patients with idiopathic Parkinson's disease were severely disabled or dead after 0–5 years, with percentages rising to 60% and 80% after 5–9 years and 10–14 years duration respectively. More favourable outcomes were reported by Marttila and Rinne (1977); for a pre-levodopa group of 419 patients with Parkinson's disease only 13% had reached severe disability after an average duration of 7.2 years. The advent of levodopa appears to have slowed the rate of progression and significantly decreased the mortality of Parkinson's disease as evidenced from several surveys (Yahr, 1976; Diamond *et al.*, 1976). In both pre- and post-levodopa series rates of

progression in a certain percentage of cases of the disease have been observed to differ considerably from those of the majority of patients. Mjönes (1949) found 6–10% of the patients in his survey to follow a 'mild course' with only minor disability for over 10 years and Sigwald *et al.* (1959) described 'stationary' forms with little or no progression over a 7 year period in 5% of his large series of 1700 patients. Such benign courses have been observed with a similar frequency by Marttila and Rinne (1977) who also claimed this to be characteristic for Parkinson's disease with early onset (see above). On the other hand a rapid progression was seen in 6% of Marttila and Rinne's patients and Birkmayer and co-workers (1974) have suggested the delineation of a malignant type of Parkinson's disease which they observed in 10–15% of their cases. Besides the tendency for rapid deterioration these authors' criteria for malignancy of Parkinson's disease also include response characteristics to levodopa which tended to elicit less initial improvement and a faster loss of efficacy with the early development of response fluctuations, dyskinesias and drug-induced psychoses. Among the clinical criteria that were frequently found to be associated with either slow or rapid progression predominant tremor or tremor-onset appeared to be prognostically favourable while an akinetic-rigid pattern tends to imply more rapid progression (Pollock and Hornabrook, 1966; Hoehn and Yahr, 1967; Marttila and Rinne, 1977; Barbeau and Roy, 1984). In a survey of 196 the author's own patients with idiopathic disease, 20 cases (10.2%) followed a malignant course of disease with the development of severe disability, Hoehn and Yahr Stages IV & V, within 5–9 years after the onset of symptoms despite early treatment with maximum tolerated doses of levodopa (Poewe and Gerstenbrand, 1986). The mean age at onset did not differ significantly from that of the total group. An akinetic-rigid pattern of the disease with little or no tremor was present in 11 cases (55%) while 9 showed the classical triad

Table 11.4 'Malignant course' of disease in 196 patients with idiopathic Parkinson's disease

Number	20 cases (10.2%)
Mean age	63 (± 1.3) years
Duration	5.4 (± 1.2) years
Clinical profile	
Akinetic-rigid	11 cases (55%)
'Classical'	9 cases (45%)
Associated dementia	5 cases (25%)

of akinesia, rigidity and tremor (see Table 11.4). It is noteworthy that no tremor-dominant cases were found in this category as opposed to 24% of the total sample presenting in that manner. In addition, severe dementia was present in 5 (25%) of the 'malignant' cases while only 8% of the total group of patients had that degree of mental impairment. These observations may be construed as further evidence for an association between akinetic-rigid presentation and rapid deterioration of Parkinson's disease, and also indirectly for a more favourable prognosis for tremor-dominant cases. As has been pointed out by others (Pollock and Hornabrook, 1966; Birkmayer *et al.*, 1974; Lieberman *et al.*, 1979) there also seems to be an association between dementia and rapid progression.

The levodopa response of Parkinson's disease has frequently been described as more dramatic with respect to reduction of akinesia than for relief of tremor (Birkmayer and Hornykiewicz, 1961; Birkmayer and Riederer, 1983; Siegfried, 1976). Analysing the long-term results of levodopa treatment in a group of patients with idiopathic Parkinson's disease the authors found that among patients who had developed drug-induced abnormal involuntary movements (AIMs) there was a different distribution of patterns of cardinal symptoms as compared to those patients without AIMs (Poewe and Gerstenbrand, 1986). While the classical picture of similar expression of rigidity, akinesia and tremor was found in approximately 50% of patients with and without levodopa-induced AIMs, akinetic-rigid cases were more frequently encountered among those with dyskinesia than among those without this side-effect. In a group of patients with disabling dyskinesia, akinetic-rigid cases made up to 70% of all patients (see Table 11.5); on the other hand tremor-dominant cases were almost absent in the group with levodopa-induced AIMs. There were no significant differences with respect to age, duration of disease or mean levodopa dosage among those with or without dyskinesia. The mean duration of treatment, however, was shorter in the group without AIMs as compared with the dyskinetic group. It was concluded that there is a correlation between an akinetic-rigid pattern of Parkinson's disease and the tendency to develop levodopa-induced AIMs.

Considering the tendency for more rapid progression of akinetic-rigid Parkinson's disease, as discussed earlier, severity of nigral cell loss may be the underlying determining factor for this correlation. Severity of nigral damage was held responsible for the early onset of drug-induced dyskinesias and response fluctuations within weeks and months after initiation of levodopa treatment in a recent report of patients with MPTP-induced parkinsonism (Langston and Ballard, 1984).

In trying to summarize the observations outlined above, one may postulate a clinical subtype of idiopathic disease which is characterized by rapid progression and a limited response to levodopa with early

Table 11.5 Classification according to abnormal involuntary movements (AIMs)

	Without AIMs		*With AIMs*	
	Total (n=78)	*levodopa: 5 years (n=23)*	*Total (n=34)*	*Disabling AIMs*
Age (years)	65.1 ± 6.9	66.5 ± 7.1	66.3 ± 8.6	63.9 ± 7.4
Disease duration (years)	9.8 ± 4.1	10.2 ± 3.7	11.1 ± 7.1	12.8 ± 5.6
Mean levodopa dose (mg)	690 ± 321	710 ± 242	890 ± 432	917 ± 514
Treatment duration (years)	3.7 ± 1.97	6.3 ± 1.0	5.3 ± 2.7	8.7 ± 4.0
Type				
ART	36 (46%)	11 (48%)	19 (56%)	6 (30%)
AR	21 (27%)	4 (17%)	14 (41%)	14 (70%)
T	21 (27%)	8 (35%)	1 (3%)	NONE

ART = akinesia, rigidity and tremor, AR = akinesia and rigidity, T = tremor.

development of dose-limiting dyskinesia and response fluctuations; akinetic-rigid features tend to predominate over tremor. The pathological features of this type are as yet unknown but they may include factors of severity and speed of nigral degeneration.

11.2.3 Variability of mental changes

It is now well established that dementia and depression may form part of the clinical picture in certain patients with idiopathic Parkinson's disease (Chapter 13). There is, however, a wide variation among the reported occurrence rates. For dementia, figures range from less than 10% to 81%. In a recent review of 17 major studies over the past 60 years Brown and Marsden (1984) discussed some of the possible reasons for this variability including problems of diagnosis and assessment of dementia as well as variability of patient sampling. Taking into account the possibility of misdiagnosis they estimated a prevalence of 15–20% rather than the average 31.5% calculated from reports in the literature. An even lower figure of 3–14% was found by Lees (1985) when he re-evaluated data from a community-based epidemiological study restricted

to patients wtih idiopathic disease. One factor in the variability of patient sampling that may not have received sufficient attention in previous studies is the possibility that dementia may be a feature of only certain types of Parkinson's disease. Marttila and Rinne (1976b) for example, found a significant correlation of dementia with akinesia and rigidity but not with tremor in their epidemiological survey of 445 Parkinsonian patients, 421 of whom belonged to the idiopathic variety. Similar correlations of dementia and cognitive deficits with bradykinesia and rigidity have been reported by others (Mayeux *et al.*, 1981; Mortimer *et al.*, 1982; Piccirilli *et al.*, 1984). In the author's series of 196 patients with idiopathic disease cited earlier in this chapter, 155 cases had been assessed for intellectual impairment by a mini-mental state examination and by evaluating information obtained from close relatives. Based on that information a diagnosis of severe dementia was possible in 13 cases (8%). Nearly 50% of the demented patients exhibited a predominantly akinetic-rigid parkinsonian syndrome as opposed to only 19% of the cases in the non-demented group (Table 11.6). Tremor-dominant cases

Table 11.6 Dementia in 155 patients with idiopathic Parkinson's disease

Dementia	*Nil*	*Mild*	*Severe*
Number	105 (68%)	37 (24%)	13 (8%)
Mean age (years)	61.0	70.4	74.0
Mean disease duration (years)	6.0	4.7	4.4
Clinical profile			
'Classical'	57 (54%)	NONE	7 (54%)
Akinetic-rigid	20 (19%)		6 (46%)
Tremor-dominant	28 (27%)		NONE

comprised 27% of non-demented patients, but could not be found among the demented. The demented group were older and had a shorter average duration of the disease than the non-demented.

It has been claimed that patients with dementia comprise a disorder clinically distinct from classical Parkinson's disease – not only because of significant intellectual impairment but also because it occurs in older age groups, is more rapidly progressive and less responsive to levodopa (Lieberman *et al.*, 1979); furthermore, Parkinson's disease with dementia tends to be associated with akinetic-rigid features. Based on pathological

studies showing concomitant Alzheimer-type changes in the hippocampus and neocortex with Lewy bodies in the brain stem, it has been postulated that Parkinson's disease with dementia represents a combination of 'Lewy body disease' with Alzheimer's disease (Hakim and Mathieson, 1979). Clinico-pathological correlations supporting this view have been proposed by Boller and co-workers (1980) who, in addition, found concomitant Alzheimer-type changes in parkinsonian brains to be 6 times greater than in an age-matched control group suggesting that the association of 'Lewy body disease' with Alzheimer's disease did not occur by chance. Other studies have, however, failed to detect Alzheimer changes in the brains of demented parkinsonians (Ball, 1984), and Yoshimura (1983) found numerous Lewy bodies in the cortex of demented parkinsonians, suggesting 'diffuse Lewy body disease' to be the basis for dementia in Parkinson's disease.

The neuropathological basis of depression in Parkinson's disease is even more obscure than that for dementia. From a clinical of view it is noteworthy that depression has been found to be negatively correlated with tremor (Vogel, 1982); indirect evidence for this may also be obtained from the depression data in our series (Table 11.7). It seems reasonable to postulate that mental changes are more likely to be encountered in akinetic-rigid cases than in tremor-dominant cases.

Table 11.7 Depression in 124 patients with idiopathic Parkinson's disease

Severity	*Absent-mild*	*Moderate*	*Marked*
Frequency	79 (64%)	38 (30%)	7 (6)%
Clinical profile			
'Classical'	32 (40%)	18 (47%)	4 (57%)
Akinetic-rigid	26 (33%)	14 (37%)	3 (43%)
Tremor-dominant	21 (27%)	6 (15%)	

11.3 PROPOSAL FOR A CLINICAL CLASSIFICATION

Based on the above evidence we propose that idiopathic Parkinson's disease be subdivided into three clinically identifiable types (see Table 11.8) which are:

1. 'classical' Parkinson's disease: with expression of akinesia, rigidity and tremor (ART-type)

2. akinetic-rigid type: with little or no tremor (AR-type)
3. tremor-dominant type: with mild akinesia and rigidity (T-type).

Such a division is similar to the former distinctions between 'paralysis agitans sine agitatione' and 'paralysis agitans sine rigiditate' cited above which now seem to be further substantiated by emerging clinical epidemiological data. The majority of patients with idiopathic Parkinson's disease can be assigned to a 'classical' variety or ART-type with pre-senile or senile onset and intially unilateral signs developing into a full clinical bilateral syndrome. A good levodopa response is usually obtained and fluctuations usually do not develop before 3–5 years of treatment; there may be associated dementia and faster deterioration with a poor levodopa response in this type of disease but it occurs less often than the akinetic-rigid type. The akinetic-rigid type of disease (AR-type) tends to have an earlier age of onset and seems to be the most frequent variant of juvenile disease. Prognostically it is less favourable and more often associated with rapid progression and poor levodopa response than the ART-type and there seems to be an earlier development of response fluctuations and abnormal involuntary movements after long-term levodopa treatment. Dementia tends to be associated with this type of disease. The tremor-dominant type of parkinsonism (T-type) is prognostically the most favourable variant with slower progression and less likelihood of severe disability than the other two variants. Tremor-dominant disease seems to be less commonly associated with dementia or depression and according to some authors may be related to essential tremor (Barbeau and Pourcher, 1982; Barbeau and Roy, 1984). Epidemiological studies have, however, so far failed to detect an increased prevalence of Parkinson's disease in families with essential tremor (Larsson and Sjogren, 1969; Marttila *et al.*, 1984); on the other hand, action and postural tremor is not uncommon in Parkinson's disease nor is slight rigidity in essential tremor so that possible pathological and pathoshysiological links between the two conditions merit further exploration.

These three variants can be distinguished in the common pre-senile or senile forms of idiopathic Parkinson's disease. Whether similar aspects apply to the rarer juvenile or early onset form of the disease where symptoms start before age 40 years is difficult to judge because of the paucity of available clinical and epidemiological studies. It seems from published reports that early-onset Parkinson's disease shares certain characteristics with the akinetic-rigid type of pre-senile or senile disease. However, Barbeau and Pourcher (1982) have suggested a familial form of early Parkinson's disease with two sub-groups: a familial akinetic-rigid group and a familial essential tremor-related, tremor-onset

group. Despite the uncertainties concerning the nosological position of the juvenile disease for the moment it seems justifiable to delineate it from pre-senile or senile Parkinson's disease as set out in Table 11.8.

Table 11.8 Clinical classification of idiopathic Parkinson's disease

(1) Pre-senile and senile disease
(a) 'Classical' (ART-type)
(b) Akinetic-rigid (AR type)
(c) Tremor-dominant (T type)
(2) Juvenile or early-onset

11.4 CONCLUSIONS

There are evident limitations to clinical subdivisions of idiopathic Parkinson's disease as proposed in Table 11.8. One is that a given patient cannot be confidently classified at an early stage of his disease or at least until the full clinical profile, rate of progression and response to therapy can be assessed; a certain degree of type overlap is also to be expected. However, the proposed classification may prove to be a useful basis for future studies of particular aspects of idiopathic Parkinson's disease such as the spectrum of associated symptoms, possible role of genetic factors, natural history, response to different therapies and, probably most important, clinicopathological correlations. From the evidence available it appears that there might be three main pathological patterns of Parkinson's disease, as listed in Table 11.9 (Forno and Ellsworth, 1971; Alvord *et al.*, 1975; Hakim and Mathieson, 1979; Yoshimura, 1983) and it remains to be determined whether or not correlations can be established between the clinical types proposed in Table 11.8 and the pathological classification of Table 11.9.

Table 11.9 Pathological classification of idiopathic Parkinson's disease

(1) Lewy body disease
(a) Brain-stem restricted
(b) Diffuse
(2) Neurofibrillary tangle disease
(3) Combination of (1) and (2)

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