Ullmain's Encyclopedia of Industrial Chomistry

Fifth, Completely Revised Edition

Volume A 19: Parkinsonism Treatment to Photoelectricity

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Volume A 19: Parkinsonism Treatment to Photoelectricity

Editors: Barbara Elvers, Stephen Hawkins, Gail Schulz





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Symbols and Units

Symbols and units agree with SI standards (for conversion factors see pp. VIII - IX). The following list gives the most important symbols used in the encyclopedia. Articles with many specific units and symbols have a similar list as front matter.

Symbol	Unit	Physical Quantity		
$a_{\mathbf{B}}$		activity of substance B		
$A_{\rm r}$		relative atomic mass (atomic weight)		
À	m² -	area		
C _B	mol/m ³ , mol/L (M)	concentration of substance B		
\check{C}	\mathbf{C}/\mathbf{V}	electric capacity		
C_{p} , C_{r}	J kg ¹ K ⁻¹	specific heat capacity		
d'	cm, m	diameter		
d		relative density $(\varrho/\varrho_{water})$		
D	m^2/s	diffusion coefficient		
- D	Gy (= J/kg)	absorbed dose		
e e	2) ("IME!	elementary charge		
E	J	energy		
E E	V/m	electric field strength		
Ë	V	electromotive force		
	j	activation energy		
$\frac{E_{\Lambda}}{\epsilon}$	J			
f	C21 1	activity coefficient		
F	C/mol	Faraday constant		
F	N	force		
₹	m/s ²	acceleration due to gravity		
G	J	Gibbs free energy		
h	m	height		
h	$\mathbf{W}\cdot\mathbf{s^2}$	Planck constant		
H	J	enthalpy		
1	Α	electric current		
ľ	cd	luminous intensity		
((variable)	rate constant of a chemical reaction		
ķ	J/K	Boltzmann-constant		
K	(variable)	equilibrium constant		
1	m	length		
) 1	g, kg, t	mass		
 Λ 1 ,	EE	relative molecular mass (molecular weight)		
η_D^{20}		refractive index (sodium D-light, 20 C)		
'1) 1	mol	amount of substance		
N _A	mol "1	Avogadro constant $(6.023 \times 10^{23} \text{ mol}^{-1})$		
=		=		
()	Pa; bar*	pressure		
5	J	quantity of heat		
*	m	radius		
R	J.K. ¹mol "¹	gas constant		
R	Ω	electric resistance		
S	J/K	entropy		
1	s, min, h, d, month, a	time		
,	C	temperature		
T	K	absolute temperature		
u	m/s	velocity		

^{*} The official unit of pressure is the pascal (Pa).

Symbols and units (continued from p. VII)

Symbol	Unit	Physical Quantity
\overline{U}	V	electric potential
U	J	internal energy
V	m³, L, mL	volume
W'		mass fraction
W	J	work
$X_{\mathbf{B}}$	`	mole fraction of substance B
α		cubic expansion coefficient
x	W m - 2 K - 1	heat-transfer coefficient (heat-transfer number)
α		degree of dissociation of electrolyte
[α]	$10^{-2} \text{deg cm}^2 \text{g}^{-1}$	specific rotation
17	Pa·s	dynamic viscosity
θ	°C	temperature
×		c_{p}/c_{v}
λ	Wm ⁻¹ K ⁻¹	thermal conductivity
λ	nnı, m	wavelength
μ		chemical potential
ν	Hz; s ⁻¹	frequency
V	m²/s	kinematic viscosity (η/ϱ)
π	Pa	osmotic pressure
Q	g/cm ³	density
σ	N/m	surface tension
τ	$Pa(N/m^2)$	shear stress
φ		volume fraction
X	$Pa^{-1} (m^2/N)$	compressibility

Conversion Factors

SI unit	Non-SI unit	From SI to non-SI multiply by
Mass		
kg	pound (avoirdupois)	2.205
kg	ton (long)	9.842×10^{-4}
kg	ton (short)	1.102×10^{-3}
Volume		
m^3	cubic inch	6.102×10^4
m ³	cubic foot	35.315
m^3	gallon (U.S., liquid)	2.642×10^2
m^3	gallon (Imperial)	2.200×10^2
Temperature		
°C	" F	$C\times 1.8+32$
Force		
N	dyne	1.0×10^{5}

Conversion factors (continued from p. VIII)

SI unit	Non-SI unit	From SI to non-SI multiply by	
Energy, Work			
J	Btu (int.)	9.480×10^{-4}	
3	cal (int.)	2.389×10^{-1}	
j	eV	6.242×10^{18}	
J	сгд	1.0×10^7	
J	$\mathbf{k}\mathbf{\hat{W}}\cdot\mathbf{h}$	2.778×10^{-7}	
J	kp · m	1.020×10^{-1}	
Pressure			
MPa	at	10.20	
MPa	atm	9.869	
MPa	bar	10	
kPa	mbar	10	
kPa	min Hg	7.502	
kPa	psi	0.145	
kPa	to r r	7.502	

Prefixes for Powers of Ten

E (exa)	1018	M (mega) 106	d (deci)	10-1	n (nan o) 10 °
P (peta)	$10^{1.5}$	k (kilo) - 10 ³	c (centi)	10-2	p (pico) 10 ⁻¹²
T (tera)	1012	h (hecto) 10 ²	m (milli)	10-3	f (femto) 10 15
G (giga)	109		μ (micro)	10-6	a (atto) 10 18

Abbreviations

The following is a list of the abbreviations used in the text. Common terms, the names of publications and institutions, and legal agreements are included along with their full identities. Other abbreviations will be defined wherever they first occur in an article. For further abbreviations, see p. VII (Symbols and Units), p. XIV (Companies and Country Codes in Patent References). The names of periodical publications are abbreviated exactly as done by Chemical Abstracts Service.

abs. a.c.	absolute alternating current		of dangerous goods on the Rhine and all national
ACGIH	American Conference of Govern- mental Industrial Hygienists		waterways of the countries concerned)
ACS	American Chemical Society	ADP	adenosine 5'-diphosphate
ADI	acceptable daily intake	ADR	accord européen relatif au
ADN	accord curopéen relatif au trans- port international des marchand- ises dangereuses par voie de navigation interieure (European agreement concerning the international transportation		transport international des marchandises dangereuses par route (European agree- ment concerning the inter- national transportation of dangerous goods by road)
	of dangerous goods by inland waterways)	AEC	Atomic Energy Commission (United States)
ADNR	ADN par le Rhin (regulation	AIChE	American Institute of Chemical
	concerning the transportation		Engineers

X Abbreviations Vol. A 19

AIME Metallurgical, and Petroleum Engineers AMP adenosine 5'-monophosphate AphA American Parmaceutical decomp. Association API American Petroleum Institute AsTM American Petroleum Institute AsTM American Petroleum Institute AsTM American Society for Testing and Materials DIN Deutsche Forschungsgemeinschaft (German Science Foundation) dilute, diluted dilute, diluted Deutsche Industrie Norm (Federal Republic of Germany) dimethylformamide decoxyribonucleic acid DPF Department of Energy (United States) BAM Bundesanstalt für Material-prüfung (Federal Republic of Germany) DOE Department of Energy (United States) Beilstein Biologischer Arbeitsstoff-Toleranzwert (biological tolerance value for a working material, established by MAK commission, see MAK) Beilstein Beilstein's Handbook of Organic Chemistry, Springer, Berlin Heidelberg New York ed. European Community editor, edito
AMP APhA American Pharmaceutical APhA American Pharmaceutical Association API American Petroleum Institute ASTM American Society for Testing and Materials ATP Adenosine 5'-triphosphate BAM Bundesanstalt für Material- prüfung (Federal Republic of Germany) BAT Biologischer Arbeitsstoff-Toleranz- wert (biological tolerance value for a working material, established by MAK commission, see MAK) Beilstein Beilstein Beilstein Beilstein Brunauer Emmett Teller BGBl. Bundesgesetzblatt (Federal Republic of Germany) BIOS British Intelligence Objectives Sub- committee Report (see also FIAT) BOD Biritish Pharmacopeia BS British Standard Ca. circa calcd. Calculated CAS Chemical Abstracts Service cat. cafel Calculated CAS Chemical Abstracts Service cat. cafel Cermany Chemistry. Calculated CAS Chemical Abstracts Service cat. catalyst; catalyzed cef. Compare decompose, decomposition decompose, decomposition decompose, decomposition decompose, decomposition decompose, decomposition Deutsche Forschungsgemeinschaft (German Science Foundation) dilute, dilute, diluted dilute, diluted dilute, diluted dilute, diluted dilute, diluted DIN Deutsche Forschungsgemeinschaft (German Science Foundation) dilute, diluted dilute, dilute, dilutes dilute, dilute, dilutes dilute, dilutes despurates (Federal Republic of Germany) DF DPD Department of Transportation Materials
APhA American Pharmaceutical Association Association DFG Deutsche Forschungsgemeinschaft (German Science Foundation) ASTM American Petroleum Institute ASTM American Society for Testing and Materials DIN Deutsche Industrie Norm (Federal Republic of Germany) BAM Bundesanstalt für Material-prüfung (Federal Republic of DNA deoxyribonucleic acid Germany) BAT Biologischer Arbeitsstoff-Toleranzwert (biological tolerance value for a working material, established by MAK commission, see MAK) Beilstein Beilstein's Handbook of Organic Chemistry, Springer, Berlin Heidelberg New York EBT Brunauer Emmett Teller e.g. for example emf clectromotive force EN European Standard (European Standard (European BIOS British Intelligence Objectives Subcommittee Report (see also FIAT) BOD biological oxygen demand bp boiling point EPA British Standard ESCA Chemical Abstracts Service cat. catalyst; catalyzed ef. compare
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cf. compare et al. and others
Ci. Compare
CFR Code of Federal Regulations etc. et cetera
(C. L. ED. LV. (C.C.)
() and household are and
Chemic Chemikanengesetz (redetat Ke
public of Cermany)
C.I. Colour Index FDA Food and Drug Administration
CIOS Combined Intelligence Objectives- (United States)
Subcommittee Report (see also FD & C Food Drug and Cosmetic Act
FIAT) (United States)
CNS central nervous system FHSA Federal Hazardous Substances
Co. Company Act (United States)
COD chemical oxygen demand FIAT Field Information Agency, Techni-
conc. concentrated cal (United States reports on the
const. constant chemical industry in Germany, 1945)
Corp. Corporation Fig. figure
crit. critical fp freezing point
CTFA The Cosmetic, Toiletry and Friedländer P. Friedländer, Fortschritte der
Fragrance Association (United Teerfarbenfabrikation und
States) verwandter Industriezweige,

Vol. A19 Abbreviations XI

	Vol. 1 - 25, Springer,	i.m.	intramuscular
	Berlin 1888 - 1942	IMDG	International Maritime Danger-
FT	Fourier transform		ous Goods Code
(g)	gas, gaseous	IMO	Inter-Governmental Maritime
GC	gas chromatography		Consultive Organization (in the
GefStoffV	Gefahrstoffverordnung (regula-		past: IMCO)
	tions in the Federal Republic of	Inst.	Institute
	Germany concerning hazardous	i.p.	intraperitoneal
	substances)	IR	infrared
GGVE	Verordnung in der Bundes-	ISO	International Organization for
	republik Deutschland über		Standardization
	die Beförderung gefährlicher	IUPAC	International Union of Pure and
	Güter mit der Eisenbahn (regula-		Applied Chemistry
	tion in the Federal Republic of	i.v.	intravenous
	Germany concerning the trans-	Kirk-	Encyclopedia of Chemical Tech-
	portation of dangerous goods by	Othmer	nology, 3rd ed., J. Wiley & Sons,
	rail)	Othinei	New York - Chichester Brisbane
GGVS	Verordnung in der Bundes-		Toronto 1978 ~ 1984
	republik Deutschland über die	415	
	Beförderung gefährlicher Güter	(l)	liquid
	auf der Straße (regulation in the	Landolt-	Zahlenwerte u. Funktionen aus
· ·	Federal Republic of Germany	Bornstein	Physik, Chemie, Astronomie.
	concerning the transportation of	٠.	Geophysik u. Technik, Springer,
	dangerous goods by road)		Heidelberg 1950 1980;
GGVSee	Verordnung in der Bundes-		Zahlenwerte und Funktionen
	republik Deutschland über die		aus Naturwissenschaften und
	Beförderung gefährlicher Güter		Technik, Neue Serie, Springer,
	mit Seeschiffen (regulation in the		Heidelberg, since 1961
	Federal Republic of Germany	LC_{50}	lethal concentration
•	concerning the transportation of	LCLo	lowest published lethal
	dangerous goods by sea-going		concentration
	vessels)	LD_{50}	lethal dose
GLC	gas-liquid chromatography	LDLo	lowest published lethal dose
Gmelin	Gmelin's Handbook of Inorganic	In	logarithm (base e)
	Chemistry, 8th ed., Springer,	LNG	liquefied natural gas
	Berlin - Heidelberg - New York	log	logarithm (base 10)
GRAS	generally recognized as safe	LPG	liquefied petroleum gas
Hal	halogen substituent (-F, -Cl,	M	mol L
	$-\mathrm{Br}, -1$		
Houben-	Methoden der organischen	M	metal (in chemical formulas)
Weyl	Chemie, 4th ed., Georg Thieme	MAK	Maximale Arbeitsplatz-
	Verlag, Stuttgart		Konzentration (maximum con-
HPLC	high performance liquid		centration at the workplace in the
	chromatography		Federal Republic of Germany);
IARC	International Agency for Re-		cf. Deutsche Forschungsgemein-
* . * .	search on Cancer, Lyon, France		schaft (ed.): Maximale Arbeits-
IAEA	International Atomic Energy		platzkonzentrationen (MAK) und
7474 500	Agency		Biologische Arbeitsstoff-
IATA-DGR	International Air Transport		Toleranz-Werte (BAT), VCH
	Association, Dangerous Goods		Verlagsgesellschaft, Weinheim
1040	Regulations		(published annually)
ICAO	International Civil Aviation	max.	maximum Munufacturing Chamists
•	Organization	MCA	Manufacturing Chemists
i.e.	that is		Association (United States)

XII Abbreviations Vol. A 19

Methodicum Chimicum, Georg Thieme Verlag, Stuttgart maximale Immissionskonzentration (maximum immission concentration) minimum minimum mething point mass spectrum than the point mass spectrum, mass spectrometry NAS National Academy of Sciences (United States) NASA National Academy of Sciences (United States) NASA National Bureau of Standards (United States) NEC National Collection of Type Cultures (United States) NIDSH National Institute of Health (United States) NROSH National Research Development Corporation (United States) NRC Nuclear Regulatory Commission (United States) NRC National Science Foundation (United States) NSC National Science Foundation (United States) NSC National Science Foundation (United States) NSF (United States) NSF (Department of Commerce, Scientific and Industrial Reports (Cooperation and Development Cooperation and Development Cooperation and Science Foundation (Eds.) Patty Industrial Hygiene and Toxicology, 3rd ed., Wiley Interscience, New York Publication Beard Report (U.S. Department of Commerce, Scientific and Industrial Regions) PB report European Pharmacopoeia, 2nd ed., Council of Furope, Strasbourg 1981 part per hundred rubber (resin) pprip part per hundred rubber (resin) pprip part, per nillion MICH National Concertain Acidemy of Science (City) and the and and concertain and Development of Commerce, Scientific and Industrial Regions (City) and the propagation of Cernany (City) and the propagation of Cernany (City) and the propagation of Cernany (City) and City and Cit	Me	methyl substituent (CH ₃)	q. v.	which see (quod vide)
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Ullmann	Ullmanns Encyklopädie der Technischen Chemie, 4th ed., Verlag Chemie, Weinheim 1972–1984; 3rd ed., Urban und Schwarzen-		for storage, filling, and transpor- tation of flammable liquids, clas- sification according to the flash point of liquids, recently in ac- cordance with the classification in
USAEC	berg, München 1951 – 1970 United States Atomic Energy		the United States)
CISITEX	Commission	VDE	Verband Deutscher Flektro-
USAN	United States Adopted Names		ingenieure (Federal Republic of
USD	United States Dispensatory		Germany)
USDA	United States Department of	ICIV	Verein Deutscher Ingemeure
	Agriculture		(Federal Republic of Germany)
U.S.P.	United States Pharmacopeia	vol	volume
UV	ultraviolet	vol.	volume (of a series of books)
UVV	Unfallverhütungsvorschriften der	VS.	versus
	Berufsgenossenschaft (workplace	WHO	World Health Organization
	safety regulations in the Federal		(United Nations)
	Republic of Germany)	Winnacker-	Chemische Technologie.
VbF	Verordnung in der Bundesrepublik	Küchler	Carl Hanser Verlag,
	Deutschland über die Errichtung		München
	und den Betrieb von Anlagen zur	wt	weight
	Lagerung, Abfüllung und Beför-	\$	U.S. dollar, unless otherwise stated

Abbreviations for the Names of Frequently Cited Companies

Air Products	Air Products and Chemicals	ICI	Imperial Chemical Industries
Akzo	Algemene Koninklijke Zout	IFP	Institut Français du Pétrole
	Organon	INCO	International Nickel Company
Alcoa	Aluminum Company of	3M	Minnesota Mining and Manu-
	America		facturing Company
Allied	Allied Corporation	Mitsubishi	Mitsubishi Chemical
Amer.	American Cyanamid	Chemical	Industries
Cyanamid	Company	Monsanto	Monsanto Company
BASF	BASF Aktiengesellschaft	Nippon	Nippon Shokubai Kagaku
Bayer	Bayer AG	Shokubai	Kogyo
BP	British Petroleum Company	PCUK	Pechiney Ugine Kuhlmann
Celanese	Celanese Corporation	PPG	Pittsburg Plate Glass
Daicel	Daicel Chemical Industries		Industries
Dainippon	Dainippon Ink and	Searle	G.D. Searle & Company
	Chemicals Inc	SKF	Smith Kline & French
Dow Chemical	The Dow Chemical		Laboratories
	Company	SNAM	Societá Nazionale
DSM	Dutch Staats Mijnen		Metandotti
Du Pont	E.I. du Pont de	Sohio	Standard Oil of Ohio
	Nemours & Company	Stauffer	Stauffer Chemical Company
Exxon	Exxon Corporation	Sumitomo	Sumitomo Chemical Company
FMC	Food Machinery & Chemical	Toray	Toray Industries Inc.
	Corporation	UCB	Union Chimique Belge
GAF	General Aniline & Film	Union Carbide	Union Carbide Corporation
	Corporation	UOP	Universal Oil Products
W.R. Grace	W.R. Grace & Company		Company
Hoechst	Hoechst Aktiengesellschaft	VEBA	Vereinigte Elektrizitäts- und
IBM	International Business	•	Bergwerks-AG
	Machines Corporation	Wacker	Wacker Chemie GmbH

Country Codes

The following list contains a selection of standard country codes used in the patent references

AT	Austria	ID	Indonesia
AU	Australia	IL.	Israel
BE	Belgium	IT	Italy
BG	Bulgaria	JP	Japan*
BR	Brazil	LU	Luxembourg
CA	Canada	MA	Morocco
CH	Switzerland	NL	Netherlands *
CS	Czechoslovakia	NO	Norway
DD	German Democratic Republic	NZ	New Zealand
DE	Federal Republic of Germany	PL	Poland
	(and Germany before 1949)*	PT	Portugal
DK	Denmark	SE	Sweden
ES	Spain	SU	Soviet Union
Fl	Finland	US	United States of America
FR	France	YU	Yugoslavia
GB	United Kingdom	ZA	South Africa
GR	Greece	EP	European Patent Office*
HÜ	Hungary	WO	World Intellectual Property Organization

^{*} For Europe, Federal Republic of Germany, Japan, and the Netherlands, the type of patent is specified: FP (patent), FP-A (application), DE (patent), DE-OS (Offenlegungsschrift), DE-AS (Auslegeschrift), JP (patent), JP-Kokai (Kokai tokkyo koho), NL (patent), and NL-A (application).

Periodic Table of Elements

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Cross References

Particle Board → Wood Particle Size Analysis → 2. Particle Size Analysis, B2 Parting Agents → Release Agents Patents → 12. Information and Documentation, **B1**: \rightarrow 13. Patents, **B1** Peanut Oil → Fats and Fatty Oils Pectin → Polysaccharides Pencils → Drawing and Writing Materials Penicillin → Antibiotics Pentane-2,4-dione → Ketones Pentanes → Hydrocarbons Peptic Ulcer Treatment → Antacids and Peptic Ulcer Treatment Perchloric Acid → Chlorine Oxides and Chlorine Oxygen Acids Perlite → Silicates Peroxides → Peroxo Compounds, Inorganic Peroxycarboxylic acids → Peroxy Compounds, **Organic** Pest Control → Acaricides; → Crop Protection; → Insect Control; → Molluscicides; → Nematocides; → Rodenticides Pet Food → Foods, 1. General Survey Petrol → Motor Fuels Petroleum → Resources of Oil and Gas; → Oil, Oil Refining Petroleum Refining → Oil, Oil Refining Petroleum Resins → Resins, Synthetic Petroleum Sulfonates → Sulfonic Acids, Aliphatic and Alkyl Sulfates Phenanthrene → Hydrocarbons Phenethyl Alcohol → Flavors and Fragrances

Phenolsulfonic Acids → Benzenesulfonic Acids and Their Derivatives Phenylalanine → Amino Acids Phenyl Hydrazine → Hydrazine Pheromones → Biological Control; → Crop Protection; → Insect Control Phloroglucinol → Phenol Derivatives Phosphanes → Phosphorus Compounds, Inorganic Phosphates, Inorganic → Phosphoric Acid and Phosphates Phosphates, Organic → Phosphorus Compounds, Organic Phosphating → Metals, Surface Treatment Phosphazenes → Inorganic Polymers Phosphines → Phosphorus Compounds, Organic Phosphonium Compounds → Phosphorus Compounds, Organic Phosphorous Acid → Phosphorous Compounds, Inorganic Phosphors → Luminescent Materials Phosphorus Oxides → Phosphorus Compounds, Inorganic Phosphorus Oxychloride → Phosphorus Compounds, Inorganic Phosphorus Pentasulfide - Phosphorus Compounds, Inorganic Phosphorus Pentoxide → Phosphorus Compounds, Inorganic Photocells → Photovoltaic Cells Photodetectors → Photoelectricity

Parkinsonism Treatment

WOLFGANG SCHATTON, J. Gutenberg Universität, Mainz, Federal Republic of Germany
JOACHIM BORMANN, Max-Planck-Institut für Hirnforschung, Frankfurt am Main, Federal Republic of Germany

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1. Introduction

Parkinson's disease (PD) is one of the major degenerative neurological diseases afflicting humans, with a worldwide prevalence exceeding 1 per 1000 population. It is, however, primarily a disease of middle-aged and elderly individuals [1]. Thus, 1% of persons over 50 years of age is a sufferer, and more than 5% of those older than 60 years.

Early diagnosis is important if patients are to be relieved of both early and later symptoms with currently available therapies. Early diagnosis may also postpone development of the more distressing later manifestations of the disease. Although therapy alleviates symptoms, as well as restoring and sustaining a worthwhile quality of life for the patient, it does not appear to retard progression of the disease [2]-[5].

Clinical Diagnostic Criteria. The major clinical diagnostic criteria for PD are tremor, rigidity, akinesia, and bradyphrenia [6], [7]. Depression is the most frequent psychopathologic disorder. Reports on its frequency range from ca. 30 to 90%, strongly supporting the hypothesis that depression in idiopathic PD is due to endogenous neurophysiological defects, particularly a

reduction in the level of the neurotransmitter serotonin (5-hydroxytryptamine) in the brain.

Tremor is a major symptom; it usually begins unilaterally, often as the typical "pill-rolling" hand and arm activity. Tremor is present at rest, can be decreased or blocked by conscious will, but is aggravated by stress especially when directed motor actions are attempted.

Rigidity is reported as stiffness and cramplike pains in the limbs. A plastic resistance to passive movement is apparent on examination that, when coexisting with tremor, may appear as a "cogwheel effect".

Akinesia is the inability to translate an intended movement into real activity. The execution of movement is slow and is associated with postural changes in the neck and trunk, as well as a characteristic shuffling gait consisting of small hesitant steps that quicken to prevent falling. Coordinated simultaneous movement of the arms and legs is impossible.

Bradyphrenia is a slowness of cognitive processing associated with apathy, impaired concentration, and finally dementia. It may correlate positively with depression.

Other characteristics of PD are an expressionless masklike face with greasy skin, increased salivation, and impaired swallowing. Handwrit-

ing may become small, and speech difficulties produce a soft, monotonous voice. Sweating attacks, constipation, urinary frequency, and incontinence are not uncommon.

Pathophysiology of Parkinson's Disease. The central nervous system (CNS) defects associated with the development of PD are centered in the paired basal ganglia, including the striatum (caudate nucleus plus putamen), the globus pallidus (pallidum), the subthalamic nucleus, and the substantia nigra (Fig. 1) [8]-[10]. The latter is divided into two regions, the pars compacta and pars reticulata.

The basal ganglia belong to the extrapyramidal tract and are responsible for the transmission of cortical motor signals associated with voluntary movement (-> Neuropharmacology, A16, pp. 140-141). Parkinson's disease is one of a number of extrapyramidal disorders (i.e., neurological disorders) that arise from lesions specifically affecting the basal ganglia. Other extrapyramidal disorders include Huntington's chorea, Wilson's disease, dystonia, dyskinesia, and torticollis. Clinically, they represent combinations of abnormal voluntary movements, and disturbances in postural stability and muscle tone, and are collectively termed movement disorders.

The substantia nigra is severely damaged in PD. The basal ganglia appear to operate together with the cerebellum as interfaces between the cognitive and motor systems of the brain, converting intentions into motor actions. Destruction of any of the components of the basal gan-

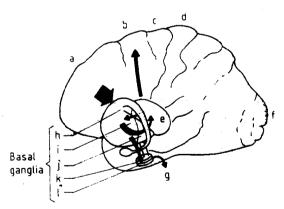


Figure 1. The basal ganglia and some of their connections [11]

a) Prefrontal cortex; b) Premotor cortex; c) Motor cortex; d) Sensory cortex; e) Thalamus, f) Visual cortex; g) Brainstem; h) Striatum (caudate nucleus); i) Striatum (putamen); j) Pallidum; k) Substantia nigra (pars compacta); l) Substantia nigra (pars reticulata)

glia, like that which occurs in the substantia nigra in PD, consequently impairs muscle function and control.

The nerve fibers of the basal ganglia are parts of input, processing, and output circuits. The input pathway from the cortex to the basal ganglia contains the largest number of neuronal fibers in the basal ganglia system. Input connections run from the cortex to the striatum (Fig. 2). The striatum in turn sends nerve fibers to dopaminesecreting nerve cells (neurons) in the substantia nigra (pars compacta). The dopamine-secreting neurons connect back to cholinergic interneurons in the striatum. The output structures of the striatum include the pallidum and the subthalamic nucleus. From here, nerve fibers project to the motor cortex via the ventrolateral thalamus to complete the overall cortex-basal gangliacortex loop. This sophisticated feedback control system works through a finely tuned balance of excitatory and inhibitory neurotransmitters. All the nerve fibers leading from the striatum to the pallidum and from there to the ventrolateral thalamus are in effect inhibitory pathways that secrete the inhibitory transmitter y-aminobutyric acid (GABA). The circular pathway cortexbasal ganglia-cortex is a feedback loop that is needed to stabilize motor control. Neurotransmission from the striatum to the substantia nigra also involves inhibitory GABA secretion at the substantia nigra nerve terminals.

The darkly staining melanophore cells in the substantia nigra send out nerve axons to the striatum to form the nigrostriatal pathway and employ dopamine as an inhibitory transmitter. Both GABA and dopamine normally control their own respective brain structures unless some disease or lesion specifically damages the pathways in which they are involved.

Another significant source of input to the striatum is the corticostriatal pathway derived from the neocortex that uses glutamate as its neurotransmitter. Glutamate is an important excitatory transmitter within the basal ganglia complex and is thought to be responsible for about half of the total input to the striatum. Acetylcholine, another excitatory neurotransmitter, is secreted from interneurons within the striatum. This interconnected system is maintained in balance via neuronal feedback control loops.

The clinical symptoms of parkinsonism are caused by destruction of the dopaminergic fibers of the darkly staining neuromelanin neurons in

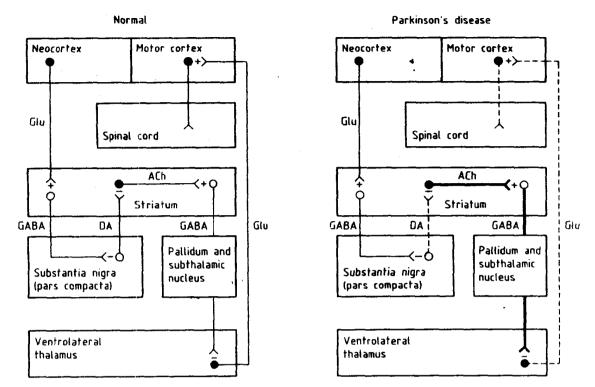


Figure 2. Schematic diagram illustrating the basal ganglia circuitry in normal humans and in patients suffering from Parkinson's disease (PD).

Excitatory (•) and inhibitory (○) neurons are shown with their axons, which form synaptic contacts with other nerve cells (+ excitatory synapse, - inhibitory synapse). Neurotransmitters secreted at the nerve terminals include γ-aminobutyric acid (GABA), dopamine (DA), glutamate (Glu), and acetylcholine (ACh). Broken and thick lines indicate reduced and increased activity, respectively. In PD, dopaminergic neurons of the substantia nigra (pars compacta) are destroyed, resulting in disinhibition (excitation) of cholinergic cells in the striatum. The overactivity of the striatal complex and its increased inhibitory output lead to a marked reduction of the activity of the thalamocortical feedback loop. These mechanisms can explain the symptoms of PD such as tremor, hypokinesia, or akinesia.

the substantia nigra (pars compacta) that project to the striatum (see Figs. 1 and 2). This destruction results in a dopamine deficiency. The cholinergic function in the striatum is simultaneously maintained, leading to an imbalance between inhibitory and excitatory neurotransmitters. A reduction in dopamine levels leads to excessive excitation by acetylcholine, which in turn augments the inhibitory (GABA) output of the striatum. As a consequence, the activity of the thalamocortical feedback loop is markedly reduced, leading to impaired motor function. Parkinson's disease can therefore be regarded as an overactivity of the striatal complex resulting from the loss of the fine control normally exercised by the neuromelanin-producing dopaminergic cells. By the time the first clinical symptoms (e.g., tremor or hypokinesia) become apparent, some 80% of these pigmented substantia nigral cells have already been destroyed.

Etiology of Parkinson's Disease. The cause of parkinsonism is not known with certainty. However, it is probably triggered by some environmental insult in early to middle life. As a result, the pigmented neurons are destroyed much sooner than in normal age-dependent degeneration. Pesticides used in rural areas (e.g., paraquat) may constitute such an environmental insult. However, the disease was known long before it was described by JAMES PARKINSON in 1817; thus, other environmental factors must also be responsible.

A recent hypothesis links PD to lipid oxidation involving excessive formation of oxygenderived free radicals in the basal ganglia. The free radicals then progressively destroy dopamine-producing neurons under participation of the immune system. Thus, Parkinson's disease is regarded as a failure of scavenger molecules produced by the basal ganglia cells to

neutralize the harmful free radical products. Further acceleration may be caused by the enzyme monoamine oxidase-B (MAO-B), which catalyzes the metabolism of catecholamine neurotransmitters and simultaneously produces reactive oxygen species. Therefore, therapeutic inhibition of MAO-B may also inhibit neurodegeneration in PD. Of major interest in this context is parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine [28289-54-5] (MPTP) because of its importance for new in vitro and in vivo pharmacological research models. This comparatively simple molecule selec-

tively destroys dopaminergic cells in the substantia nigra and induces advanced parkinsonian symptoms in humans within a few weeks. Thus, the possibility that an environmental toxin triggers the development of PD appears reasonable.

2. Therapy of Parkinson's Disease

Modern therapy started with the discovery that the brains of Parkinson patients were deficient in dopamine. Dopamine was originally re-

Figure 3. Biosynthesis and metabolism of dopamine COMT = Catechol-O-methyl transferase; MAO = Monoamine oxidase