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Idopathic Parkinsonism

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ABSTRACT:

Parkinson Disease is the brain disorder which may cause a uncontrolled movements of the body and also known for causing tremors ,shaking, abnormal movements or the balance problems. It is most common among the Geriatric The cause of PD is Idiopathic but number of many factors are characterized like environmental factors ,genetic factors, and other risk factors. There are notable differences in Parkinson's disease epidemiology according to period, place, age, sex, and ethnicity. Environmental factors may include smoking, caffeine, and the pesticides . This disorder arises due to the loss of dopaminergic neurons. This condition is not curable but they are various option for the treatment. The perception of sporadic Parkinson's disease (PD) has drastically changed in the last few decades.

KEYWORDS: Pathophsiology, Genetics, Lewy bodies, Levodopa, Etiology, Parkinsonism, Diagnosis, Treatment.

INTRODUCTION:

Dr. James Parkinson initially referred to Parkinson's disease (PD) as a "shaking palsy" in 1817. It is a neurodegenerative condition that progresses over time and has both motor and nonmotor symptoms. The disease's progressive degenerative effects on muscular control and mobility have a major clinical impact on patients, families, and caretakers (1).This neurodegenerative condition primarily manifests as a generalized slowing down of movement (bradykinesia) and at least one additional symptom of stiffness or resting tremor in later life. Constipation, excessive periodic limb movements during sleep, mood issues, excessive salivation, loss of smell, and sleep disturbances are further symptoms that are linked to this condition. (3)

The diagnosis of Parkinson's disease (PD) is still primarily clinical, and it's critical to identify early characteristics as well as symptoms and indicators of alternative parkinsonian causes (4). With over 6 million cases worldwide, Parkinson's disease is the second most prevalent neurological illness. With a prevalence rise of 2.5 times over the previous generation, Parkinson's disease is now one of the main causes of neurological disability.(5)

The trio of motor symptoms—tremor, rigidity, and bradykinesia—has historically been linked to Parkinson's disease (PD), with postural instability frequently developing as the illness worsens. On the other hand, PD is also linked to a wide range of non-motor symptoms, many of which appear years or even decades before the motor symptoms.(8) Over the age of 60, at least 1% of people are thought to have Parkinson disease. Lewy bodies and the degeneration of dopaminergic neurons in the substantia nigra are linked to the illness. The majority are idiopathic. Genetic causes account for only 10% of instances, and they are typically young people.(9)

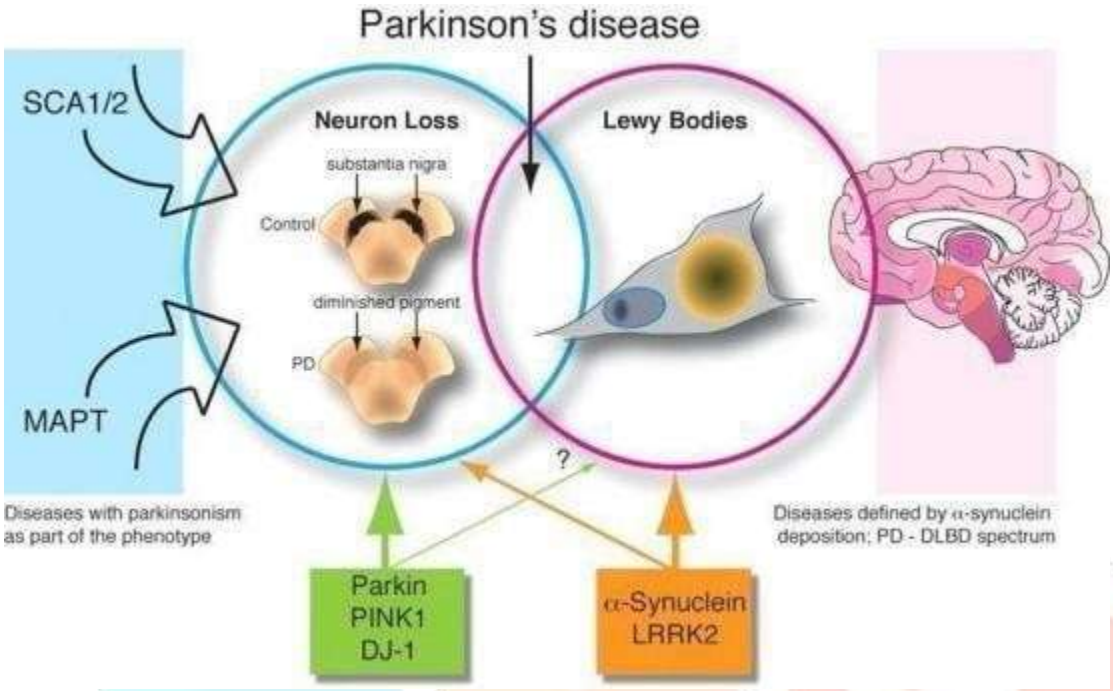

FIG.1 DISEASE WITH PARKINSONSISM AS PART OF THE PHENOTYPE (49)

EPIDEMIOLOGY :

As one ages, both the incidence and prevalence of Parkinson's disease (PD) rise, impacting 1% of those over 65.The emergence of parkinsonian characteristics prior to the age of 40 is known as early-onset Parkinson's disease (EOPD). About 3–5% of all PD cases are related to it. It is divided into two categories: "young-onset" PD (YOPD, occurring in the age range of 21–40 years) and "juvenile" PD (occurring before the age of 21).In most groups, men are twice as likely as women to get Parkinson's disease. An estimated 7–10 million people worldwide suffer from Parkinson's disease (PD), which affects men
1.5 times more often than women. A population-based investigation of Medicare beneficiaries revealed that the average frequency of PD among people 65 and older was 1.6%.(3)

At any given time, 1 to 2 persons out of every 1000 are affected by Parkinson's disease (PD); as people age, the prevalence rises to 1% of those over 60. Five to ten percent of patients are genetically predisposed. Age does really increase the incidence and prevalence of Parkinson's disease (PD); men are more likely than women to have the disorder.(9) Between the sixth and ninth decades of life, the incidence rises five to ten times. The prevalence of PD rises with age as well. Prevalence rose from less than 1% in men and women 45–54 years old to 2% in men and 4% in women 85 years of age or older in a meta-analysis of four North American groups.(34)

ETIOLOGY:

Our understanding of the etiology of Parkinson's disease has greatly advanced during the past century. The loss of pigmentation in the midbrain's substantia nigra was initially identified in 1919 as a characteristic of post-mortem brain examinations in Parkinson's disease (PD) patients.(9). It is debatable to what extent genes and environmental/lifestyle factors contribute to the pathophysiology of Parkinson's disease. Age-related biological dysfunction, such as telomere dysfunction, genomic instability, epigenetic modifications, ubiquitin-proteasome and autophagy lysosomal system, and mitochondrial abnormalities, may support and facilitate neuronal death, just like in other neurodegenerative illnesses.(10).

Pesticide and herbicide use as well as living close to industrial plants have been implicated in Parkinson's disease (PD) development. It has been observed that injections of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) can cause Parkinsonian-like symptoms in certain people. Within the mitochondria, this substance builds up. Additionally, studies point to the production of free radicals and oxidation as potential causes of thalamic nuclei damage.(9)

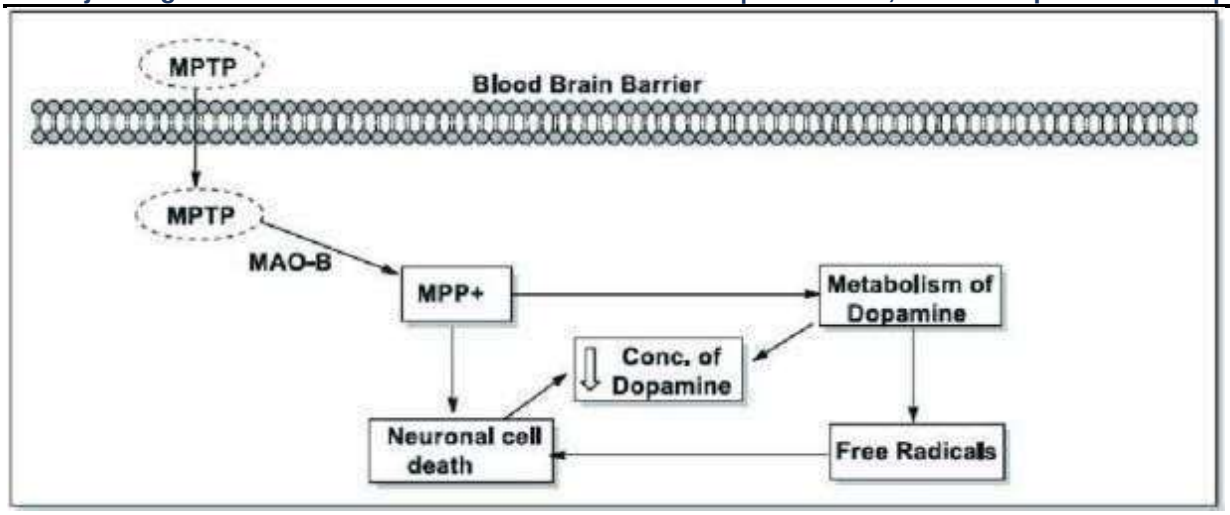

FIG.2 FLOW CHART OF THE PARKINSONS PROGRESSION(68)

When MAO-B is present, MPTP passes the blood-brain barrier and transforms into MPP+. It raises dopamine metabolism in the brain and results in the death of neurons. Dopamine metabolism also produces free radicals, which have the potential to kill neurons.(68)

What signs of Parkinson's disease are present?

Among the most common movement symptoms are the following:

- Inflexibility (hardness) .
- Bradykinesia, or sluggish movement .
- Tremors, which are uncontrollable or involuntary motions of bodily parts .
- Issues with balance and posture .
- Issues with getting about or walking .

The following symptoms of non-movement could be present:

- Pain;
- Cognitive issues (thinking ,reasoning, or memory)
- A decrease in appetite
- Constipation
- Issues with vision
- Variations in mood (anxiety, irritability)
- Issues related to sexuality
- A loss of flavor
- Smell loss (66)

GENERAL RISK FACTORS:

The most significant risk factor for Parkinson's disease (PD) is age (1, 7), with an average age of onset of 50 to 60 years. Additionally, it has been demonstrated that exposure to pesticides and family history —a genetic link—are significant risk factors. Although more risk variables have been found, it is still unknown how they can impact men and women differently
(11). The six categories of risk factors for Parkinson's disease (PD) include: medications, biomarkers, dietary factors, medical history and concomitant disorders, environmental agents, and habits. Evidence from long-term research projects (such cohort and nested case-control studies)

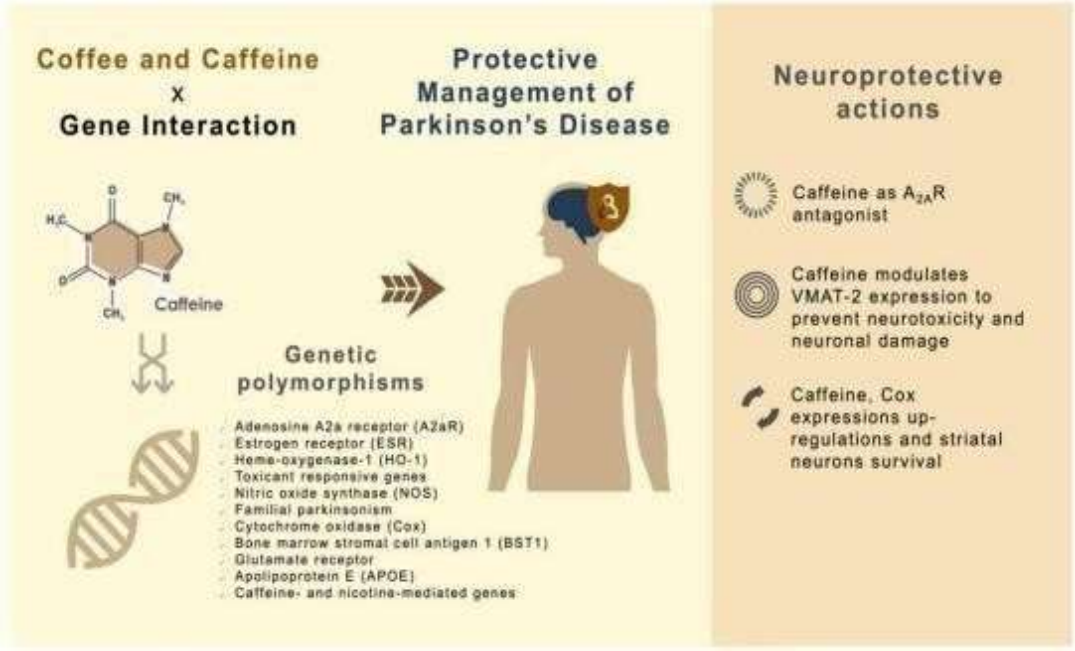

FIG.3 COFFEE AND CAFFEINE GENE INTERACTION (56)

Cigarette smoking has been extensively studied with respect to PD, with mostly consistent results. Most of the epidemiological reports are case-control studies showing a reduced risk of developing PD, with larger cohort studies also in agreement.(13). Several studies have investigated the effect of caffeine on the development of PD and reported a reduced risk of developing PD among coffee drinkers. Caffeine is an adenosine A2A receptor antagonist, which is believed to be protective in PD (15) and has been shown to be neuroprotective in a mouse model of PD (13,14).

PARKINSON'S DISORDER STAGES :

Parkinson's disease (PD) Is a degenerative neurological condition that results in the nervous system's cells breaking down. The following are PD's five stages:

Phase I

At this point, the symptoms are not severe enough to interfere with day-to-day activity.

Unilateral movement symptoms, or symptoms affecting only one side of the body, such as bradykinesia, stiffness, and tremors.

Moderate issues with balance and posture. Mild
walking difficulties .
Subtle alterations in facial expressions .

Phase II

At this point, symptoms worsen and make going about everyday tasks more challenging. But the individual can take care of himself.

Bilatera lmovement symptoms, such as bradykinesia, stiffness, and tremors, affect both sides of the body. Having trouble walking .

Challenging balance . Bad

alignment .

Lessening of the facial gestures .

Phase III

Compared to stage II, the mid-stage symptoms are more severe. The individual is still independent, though.

The two main signs of this stage are bradykinesia, or sluggish movement, and loss of balance. Eating, washing, and dressing are among the daily routines that are severely hindered.

Phase IV

At this point, the constraints in daily tasks including eating, bathing, dressing, sleeping, and awakening make independent living nearly impossible.

The individual may be able to standby themselves, but they will require help getting around. A walker could make it easier to maneuver without falling.

Phase V

At this crippling level, the symptoms could even make it impossible to get up on one's own. The individual becomes bedridden and requires transportation in a wheelchair.
Everyday tasks are hindered, necessitating a 24-hour caregiver. Among the symptoms could be the following:

- Delusions (erroneous ideas that persist in the face of contradicting information).
- Hallucinations (perceiving, sensing, or hearing unreal entities) .
- A loss of aroma .
- Constipation .
- Inadequate memory and thinking .
- Loss of weight .
- Sleep-related issues .
- Eye issues(66).

PATHOPHYSIOLOGY:

Parkinson's disease (PD) is a disorder of the extrapyramidal system, which includes basal ganglia motor structures. It is typified by a decrease in motor function resulting from dopaminergic function loss, which drives the disease's clinical characteristics (38, 39). According to additional data, Parkinson's disease (PD) may have its start in the anterior olfactory nucleus, the dorsal motor nucleus of the vagal and glossopharyngeal nerves, or the brainstem. This indicates that the disease may follow a pattern of onset in the brain stem and progress to higher cortical levels.(40)

People with Parkinson's disease (PD) lose their dopaminergic function due to progressive degradation of dopaminergic neurons in the substantia nigra pars compacta (SNpc) , which project to the striatum (the nigrostriatal pathway). Patients typically don't get the motor symptoms of Parkinson's disease (PD) until between 50% and 80% of their dopaminergic neurons have been destroyed. This suggests that a compensatory mechanism may be involved in the disease's early stages. D1 (excitatory type) and D2 (inhibitory type) dopamine receptors affect motor activity in the extrapyramidal system. This system consists of the pars reticulata section of the substantia nigra (SNpr) and the basal ganglia, which include the internal globus pallidal segment (GPi) of the ventral striatum.

Patients with Parkinson's disease (PD) have dopamine depletion in the striatum, which causes the GPi/SNpr circuits to become more active. This leads to gamma aminobutyric acid (GABA) malfunction, which in turn inhibits the thalamus. The ultimate consequence is a reduction in the thalamus's capacity to stimulate the frontal cortex, which leads to the diminished motor activity that is indicative of Parkinson's disease.

Therefore, clinical improvement in the motor symptoms of Parkinson's disease (PD) is mediated by restoring dopamine activity in the striatum through D2 and D1 receptor activation with dopaminergic treatments.(41,1)

The presence of LBs, which are defined as internal cytoplasmic aggregates made of proteins, lipids, and other components, is another important histological characteristic of Parkinson's disease (PD). Moreover, LBs have been found to be important indicators of long- term neurodegenerative illnesses, such as Parkinson's disease(47,48)

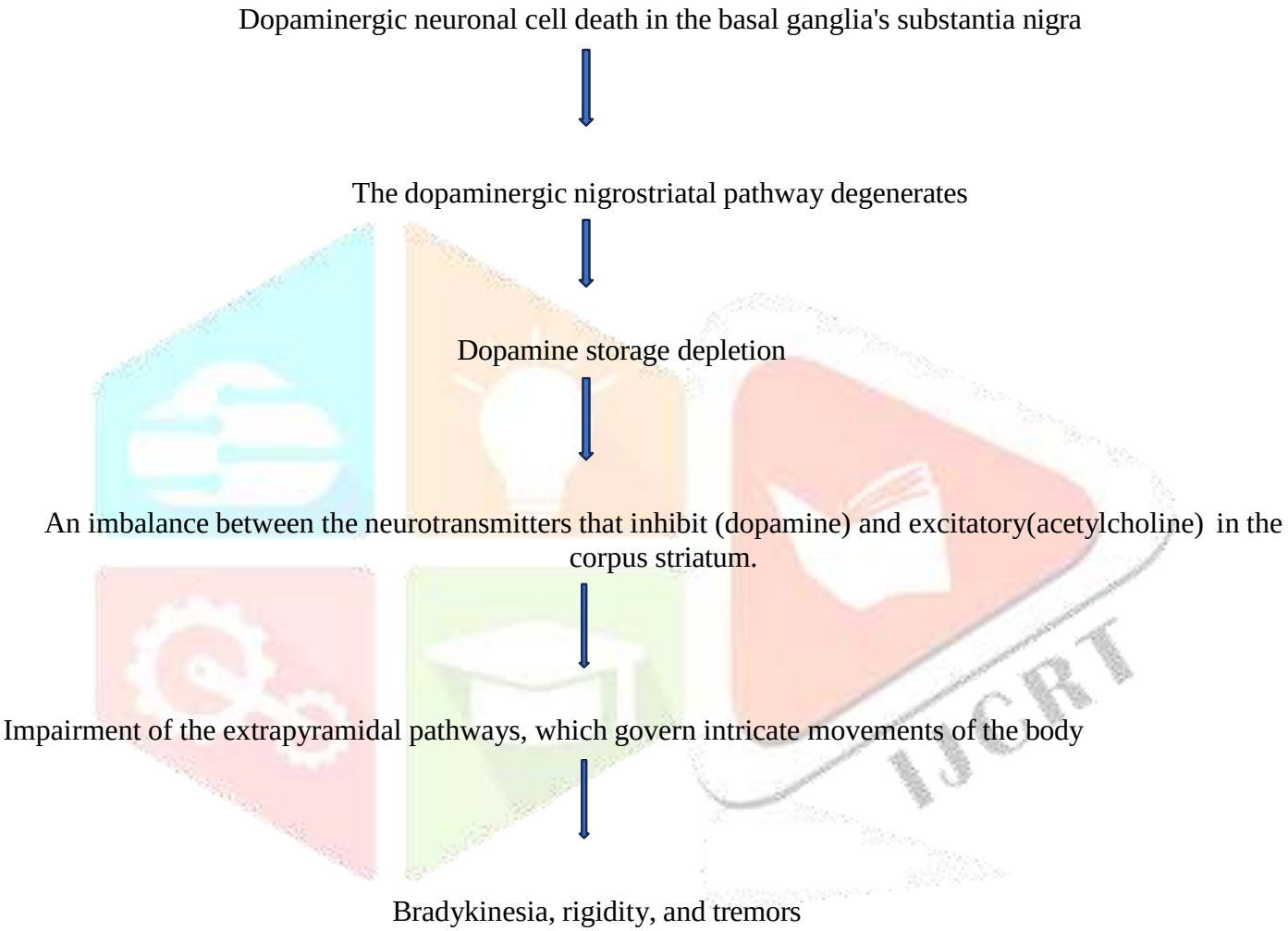

FIG.4 PATHOPHSIOLOGY OF PARKINSONS'S DISORDER (73)

LEWY BODIES:

Lewy bodies, aneosinophilic inclusions seen within neurons, are another pathologic feature of Parkinson's disease. Lewy bodies on histologic stains feature a pale halo surrounding an eosinophilic center. They are typically 5 to 25m in diameter and spherical, though they can have pleiomorphic shapes (50). They are typically found inside the cell soma, although they can also be seen free in the extracellular space or in neurites. Lewy bodies can be seen in the neocortex, diencephalon, spinal cord, and even peripheral autonomic ganglia. These brain regions are known to exhibit the greatest neuron loss in Parkinson's disease (PD). These regions include the SN, locus coeruleus, the dorsal motor nucleus of the vagus, and the nucleus basalis of Meynert.(16)

Parkinson disease dementia and dementia with Lewy bodies are the two clinical entities that makeup Lewy Body Dementia (LBD). It is a gradual degenerative brain disease with parkinsonian symptoms, psychosis, and dementia. The symptoms change overtime and varies from person to person. Since many of LBD's

symptoms are similar to those of other dementia conditions, a comprehensive clinical examination is necessary for the diagnosis. After Alzheimer's disease and vascular dementia, it is the third most prevalent kind of dementia. Alpha-synuclein and ubiquitin aggregates are seen in Lewy bodies, which are intraneuronal cytoplasmic inclusion bodies that are deposited in the brain.(44, 45, 46, 47)

GENETICS:

According to the current nomenclature for PD genetics, eighteen distinct chromosomal regions, also referred to as chromosomal loci, are numbered in chronological order of their identification (PARK1, PARK2, PARK3, etc.) and referred to as PARKs (to indicate their possible link to PD).(29).Even though Parkinson's disease (PD) is typically sporadic, an increasing number of single gene mutations have been found to cause the condition. Six genes have been found so far, including α-synuclein (SNCA), ubiquitin C-terminal hydrolase like 1 (UCH-L1), parkin (PRKN), LRRK
2, PINK 1, and DJ- 1. As of the time of writing, 11 genes have been mapped by genetic linkage.(4)

PD genetics are intricate. Common variations can interact with other genetic variables and environmental circumstances,potentiallyincreasingtheriskofParkinson'sdisease(PD).Arecentbiggenome wide association study (GWAS) found 70 loci associated with Parkinson's disease (PD) risk.(33, 35)

PARKINSON'S DISEASE-RELATED GENE MUTATION (1,51,52,53,54,55)

The gene for alpha-synuclein (SNCA)

The gene known as EIF4G1, or eukaryotic translation initiation factor 4

gamma l. The GBA gene (glucocerebrosidase)

Genelociforleucine-richrepeatkinase2(LRRK2)

Gene loci for putative kinase 1 (PINK1) triggered by PTEN The SOD2 gene (superoxide dismutase 2)

GENETICS IN INDIA:

Among Indian case series, the Parkin gene has the greatest reported mutation rate, ranging from 1.96% to39.1%.[14] InDJ1,PINK1,LRRK2,and SNCA, mutations are less common and missing. Autosomal recessive (AR) early onset Parkinson's disease (PD) has been linked to mutations in the Parkin gene, which produce significant variation in people from different parts of India.[15– 19]. (2)

WHO GETS THE PARKINSON DISEASE?

In early-and late-onset Parkinson disease, the frequency of a positive family history is not statistically different. The exact cause of Parkinson disease is unknown, but it is assumed to be the result of a combination of environmental influences superimposed on genetic predisposition or susceptibility. The onset of Parkinson disease can be categorized as juvenile (age
< 21 yr), early onset (21–50yr) and late onset (generally > 60 yr).The juvenile form is rare, is often familial (in as many as 50% of cases), is most frequently associated with a parkin gene mutation and has an atypical presentation.(28)

GBA-ASSOCIATEDPD:(Glucocerebrosidase)

It has been discovered that some genes may be connected to Parkinson's disease. A close relative with

parkinsonian symptoms is present in at least 15-20% of Parkinson's disease patients. Parkinson's disease may be caused by a combination of hereditary factors. Environmental variables can also be mixed with genetic factors.(67)

Approximately 130 GBA mutations have been found in PD patients, compared to GD's higher number [30, 31]. Numerous studies have only searched for a limited set of mutations that are often associated with Parkinson's disease. Therefore, the less persistent PD-related variants might remain undiscovered. Among other mutations, c.1448 T > C (L444P) and c.1226 A
> G (N370S) are typically the most durable.

In some communities, they even account for 70 – 80% of GBA mutations associated with Parkinson's disease.(30)
AN EPIDEMIOLOGIC PERSPECTIVE ON INFECTION AND PD (28).Parkinson's disease (PD) has been linked to numerous hereditary and environmental factors. The disease is believed to be produced by a complex interplay of multiple factors that are specific to each individual. Ninety risk alleles have been discovered in the last ten years, representing a significant rise in the number of recognized genetic risk factors.(19)

Numerous environmental factors, including cigarette smoking, caffeine intake, physical activity, plasma urate, and positive associations with pesticide exposure, have been linked to a reduced risk of Parkinson's disease (PD). Additionally, there are numerous associations with less consistent evidence across multiple categories, such as dietary factors, chemical exposures, and physical and emotional trauma. [26,27]

VIRAL INFECTION AND PD RISK:

For a long time, there have been rumors that Parkinson's disease may have a viral origin. An early example that is relevant in the context of the current SARS-CoV-2 pandemic is the advent of encephalitis lethargica, a parkinsonian condition that has been loosely related (but not conclusively) to the 1918 influenza pandemic.Viruses, especially neurotropic ones, are likely the cause of Parkinson's disease (PD), although they have not received as much research attention as environmental and genetic risk factors. (19,20)

Influenza is the virus that causes parkinsonism the most frequently. The ability of each influenza virus strain to infect the central nervous system directly varies. Neurotropic organisms are those that can directly infect nervous system cells, while non-neurotropic organisms cannot. Non-neurotropic influenza viruses, such as the 1918 H1N1 virus (Spanish flu), the 1957– 1958 H2N2 virus (Asian flu), the 1968 H3N2 virus (Hong Kong flu), and the 2009 H1N1 virus (Mexican or swine flu), constitute the majority of influenza viruses that have infected people.

Based on these results, a theory has been put up that the viral based inflammation primes the central nervous system, making it more vulnerable to a later insult that would have otherwise been benign (17, 19). Based on the lack of a significant correlation between influenza infection and Parkinson's disease (PD) in a meta-analysis combining data from four small case control studies, the appearance of this influenza-associated syndrome appears to be fairly specific to the 1918 H1N1 strain of influenza (combined OR 1.95, 95%CI 0.77–4.94 for the risk of PD following influenza infection).(25)

TREATMENT OF PARKINSON'S DISEASE IN THE AYURVEDA:

With a wide range of motor and non-motor symptoms, Parkinson's disease (PD) is a complex neurodegenerative illness that calls for an individualized treatment plan. the intervention for therapy. The discovery of 1,methyl 4phenyl 1,2,5,6 tertahydropyridine (MPTP), along with the observation that it causes a clinical picture resembling Parkinson's disease and that the disease is more common in industrialized nations, lead one to speculate that the disorder is a product of the industrial revolution. Galen (AD 138201)

makes the first recorded mention of "shaking palsy" in Western medical literature, and it wasn't until centuries later that James Parkinsons wrote a thorough account of the conditionin1817.

The current authors were inspired to research the literature on ayurveda in order to get data regarding Parkinson's disease's historical occurrence. Ayurveda, the essence of an age-old medical system, is still widely used today. It is believed to have been used in India between 5000 and 3000 BC (exact date unknown).Ayurveda, supported by the government, is a viable alternative for healthcare, even in neighboring Asian nations like Nepal, Tibet, and Sri Lanka. The ayurveda medical system is an excellent complement to the allopathic (modern medicine) medical system in Burma, Malaysia, and Indonesia.(18)

AYURVEDIC REGIMENS AND MEDICINAL PLANTS FOR NEUROPROTECTIVE SYMPATOMATIC BENEFITS:

Early research on Ayurvedic medicinal herbs and other regimens, such as Panchakarma, has shown encouraging results in treating the illness .One of the regimens, medicinal oil enema (basti), has showed promise in improving the patients' crippling non-motor symptoms. A thorough discussion has been held over the effects of two medicinal plants, Curcuma longa Linn and Withania somnifera (L.) Dunal, on models associated with Parkinson's disease. Additionally, we have included a selection of medicinal plants that are most likely to be helpful in managing particular aspects of the condition, like mood disorders, osteoporosis risk, and cognitive decline.(16)

Conclusion:

If these leads are methodically further explored by well planned longer term trials, Ayurveda, with its medicinal plants and treatment techniques, can strengthen the therapeutic arsenal of Parkinson's disease (PD) to improve
clinical outcomes.(16)

Clinical diagnostic criteria for Parkinson's disease:

The International Parkinson and Movement Disorder Society (MDS) has proposed a set of criteria that essentially represent an updated version of the Queens Square Brain Bank (QSBB)Criteria, which have been the most widely used over the past few decades, in order to improve the diagnostic accuracy of a clinical diagnosis of Parkinson's disease.(5)

DIGNOSIS:

A through history and physical examination should be part of the differential diagnosis for Parkinson's disease (PD). Casesthatarechallengingordubiousshouldbereferredtoamovementdisorderspecialistforadditionalassessment. Since there are no conclusive tests to confirm a PD diagnosis, a clinical diagnosis must be made by the clinician after reviewing the patient's medical history, evaluating the patient's symptoms, and ruling out other possible diagnoses such multiple-system atrophy, DLB illness, and related conditions.(36, 37)

COMPLICATIONS:

Dementia, depression, and laryngeal dysfunction.

Dysautonomia .

Kyphosis resulting in dysfunction of the heart (3) .

CURRENT TREATMENTS :

Although there aren't any disease modifying medication available for Parkinson's disease (PD), there are treatments that can significantly reduce motor symptoms. In terms of the non-motor symptoms of Parkinson's disease, they don't really help patients clinically. In order to lessen the severity of side effects, treatment is typically started after the patient's symptoms become bothersome.(56)

LEVODOPA:

This is usually achieved pharmacologically by taking levodopa in combination with carbidoglopamol, which reduces adverse effects and increases CNS bioavailability (3). About fifty years ago, levodopa medication was introduced for Parkinson's disease, and it has completely changed the course of treatment for this difficult condition. Levodopa is still the gold standard today, despite the addition of a number of new medications to the therapeutic arsenal. When Cotzias et al. demonstrated in 1967 that oral levodopa had a significant and long-lasting impact on the symptoms of severely impaired Parkinsonian patients, the levodopa era officially began.(46)

Levodopa-based preparations are the cornerstone of today's Parkinson's disease (PD) treatment regimen, acting as a dopamine substitute in the striatum. Dopamine cannot be utilized to treat Parkinson's disease (PD) because it can not penetrate the blood-brain barrier (BBB) (57,). Levodopa, on the other hand, is a dopamine precursor that maybe given as a medication that crosses the blood-brain barrier. DOPA decarboxylase transforms it into the neurotransmitter dopamine once it has been absorbed and passed through the blood-brain barrier (56,58).

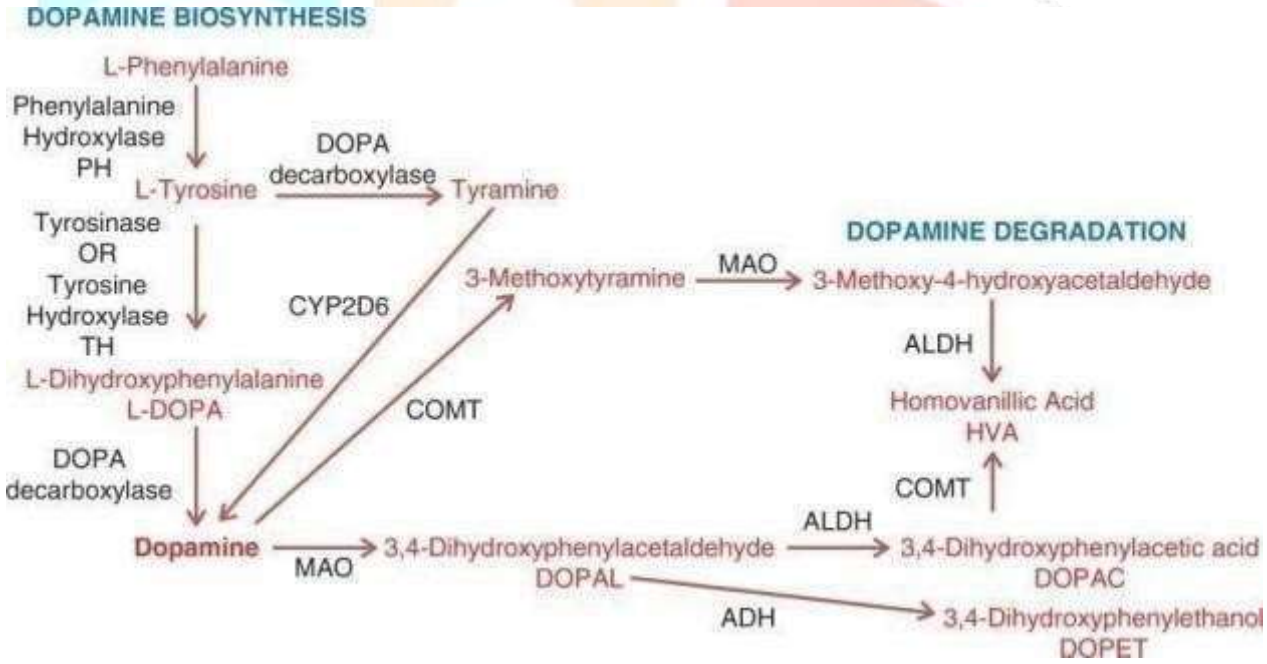

FIG.5 DOPAMINE BIOSYNTHESIS (58)

Younger people maybe started on a dopamine agonist (ropinirole, pramipexole); while it may not be as effective as levodopa, it will have less side effects. If a tremor needs to be controlled more than any other symptom, anticholinergics or amantadine maybe administered. Selegiline can help with mild symptom alleviation and is frequently used to treat early illness. The majority of antiparkinsonian drugs offer effective symptom management for three to six years. Following this time, the illness worsens and frequently becomes resistant to treatment.

Younger patients should generally receive more aggressive treatment than older individuals.(3)

Mechanism of Action :

Parkinson disease patients experience degeneration of the substantia nigra. Because of this disorder, the nigrostriatal pathway is disrupted, which lowers striatal dopamine levels. Levodopa has the ability to pass the blood-brain barrier (BBB), unlike dopamine. In the brain and peripheral nervous system, levodopa is converted to dopamine.[60,61]

In the brain and peripheral nervous system, levodopa is converted to dopamine. Levodopa is frequently given in combination with peripheral decarboxylase inhibitors (such as carbidopa and benserazide) to maximize its bioavailability and minimize its negative effects Dopamine decarboxylase inhibitors facilitate the peripheral conversion of levodopa to dopamine, hence increasing the amount of levodopa that crosses the blood-brain barrier.

It makes up for the drop in endogenous dopamine by activating postsynaptic dopaminergic receptors after it is converted to dopamine.(61)

Administration:

Oral: Often available in conjunction with benserazide or carbidopa.

- IR pills, or immediate-release
- Disintegrating tablets
- Tablets with regulated release(CR), ER (extended-release) capsules(62,63).

Small doses should be used initially; a daily dose of 300–1200 mg, or more if tolerated, split between three to twelve doses, is advised. [63] It is advised to raise the dosage by 100 mg every three or four days when following a titration regimen.
Levodopa oral dosage should be taken with meals to minimize gastrointestinal (GI) distress in Patients .Patients should take levodopa one hour before or two hour safter meals containing protein in order to increase absorption. [64]
When taking levodopa, patients should avoid eating meals high in fat or calories because this cancause a two-hour delay in absorption. Before consuming, the oral disintegrating pills must dissolve completely on the tongue. Levodopa extended- release capsules can betaken with or without food. For patients who have difficulty swallowing, the capsule can be opened, the contents sprinkled over food, and then consumed right away.(61)

Infusion: An additional mode of delivery involves a 16- hour infusion via anasojejunal tube. Studies have indicated that low plasma trough levels observed with oral medication delivery are linked to levodopa infusion. It has been demonstrated in recent research that this kind of infusion lessens the negative consequences of motor problems.
According to certain research, administering levodopa pulsates fiably may result in more motor problems than administering the medication continuously. It is not advised to provide levodopa to patients younger than18 because there is insufficient evidence on its administration in this age group.(65)

Adverse effect :

Symptoms of levodopa side effects include headache, nausea, dizziness, and somnolence. To alleviate nausea, increasing carbidopa is advised; if this doesn't work, domperidone maybe useful. Elderly patients require extra vigilance since the effects on the central nervous system (CNS) may affect them more sensitively. When elderly people take levodopa, disorientation, hallucinations, delusions, psychosis, and agitation are the most common side effects.(66, 70, 71, 72)

Contraindication:

Because levodopa use may exacerbate pre-existing neuropathy symptoms ,it is also not recommended for those with such conditions. Patients who already have a history of peptic ulcer disease are more vulnerable to GI bleeding. In individuals who have previously been diagnosed with a serious psychotic condition, levodopa may increase the chance of psychosis.(65)

Levodopa should not be administered to individuals who have a history of malignant melanoma because it may reactivate the cancer, according to the Food and Drug Administration's (FDA) label. Nevertheless, a number of research revealed that the correlation between Parkinson's disease and melanoma may account for the elevated risk of melanoma rather than drug exposure. To confirm the link between levodopa and dermatologic consequences,
more research is needed.[65,69]

Therapeutic Applications of Levodopa :

Parkinson's plus syndrome, dopa responsive dystonias, and Parkinsonism remain the main therapeutic uses of levodopa. The therapeutic efficacy of levodopa varies depending on the symptom group. Parkinson's disease specific motor symptoms, bradykinesia and stiffness, are usually improved by levodopa. Non-motor symptoms including cognitive decline, dementia, depression, psychosis, autonomic dysfunction, and sleep difficulties are not well treated by levodopa therapy. (59)

CONSULTATIONS:

Surgeon, psychiatrist, and Speech therapist, Physician, Nutritionist, Endocrinologist, Otolaryngologist(3)

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12Non-GeneticRiskFactorsforParkinson'sDisease: AnOverviewof46Systematic Reviews YancongChen,aXuemeiSun,aYaliLin,aZixuanZhang,aYinyanGao,a,*andIreneX.Y.Wua,b,*

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