

Historical Perspective of Parkinsonism and *Ra'asha*

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Unani classical literature is a rich source of information for various clinical disorders but there is a wide gap between ancient and modern views of elaborating the pathophysiology. As far as Parkinsonism is concerned, it is a syndrome characterized by tremors, muscular rigidity, Bradykinesia and postural instability. After going through literature and historical review it is very much obvious that the description about the *Ra'asha* and its associated symptoms arise due to CNS disorder that is vividly described by ancient Unani scholars but due to wide gap in ancient and modern knowledge and way of describing pathogenesis of the Parkinsonism and *Ra'asha* could not be correlated. With the help of this study a thorough review of classical literature along with model concept of extra pyramidal disorders is being incorporated.

Key words: *Ra'asha*, Parkinsonian tremors, Majon-e-jograj gogul, Extra pyramidal disorders.

Parkinson's disease is a common neurological entity found in elder people. It is characterized by tremor, rigidity, Bradykinesia and postural instability. It occurs due to the insufficient formation and action of dopamine. Human beings have always had the potential for insufficient dopamine. Although Parkinson's disease has increased in its prevalence over time, it must have existed to some extent for as long as human existence. There are references found to Parkinson's disease symptoms throughout history.

There is no elaborate description of Parkinson's disease in the Unani literature. However, while going through these, one gets enough literature under the heading of *Ra'asha* i.e. tremor. As tremor constitutes one of the important symptoms of Parkinson's disease. Parkinsonian tremor can be well visualized under the context of such descriptions, as given by Unani scholars.

Among the ancient Unani scholars, the father of medicine, Hippocrates (460 B.C.) who was the first to recognize Parkinson's disease symptoms, i.e. *Ra'asha* quoted by Zakaria al-Razi. One such quote described in *Al-Hawi Fi al-Tib* is as follows:

“*Ra'asha* occurring because of the dryness of organs is the worst type and is untreatable”¹.

Avicenna accepted the descriptions of Hippocrates about the *Ra'asha* and describes various types of *Ra'asha* with their treatment as well.

Hippocrates described, that *Ra'asha* occurs due to brain malfunction in hyperpyrexia (*Humma Muharriqa*) and disappears spontaneously.

Dioscorides (100 A.D.) has discussed the detailed treatment of *Ra'asha* in his famous book *Kitabul Hashaish* as quoted below:

“*Qurdmana* is useful in paralysis and when given with *Arq-e-karnab*, it is beneficial in tremors also. Roasted brain of wild rabbit is beneficial in *Ra'asha* occurring after chronic disease. Castorium (*Jund badaster*) is useful in *Ra'asha* in both systemic and local forms”¹.

In Roman era a lot of works were carried out on Unani system of medicine. The most famous scholar of this era is Galen. Roofus (98-117 A.D.) was also a well-known scholar during this period. While discussing *Ra'asha* he asserted that water is more beneficial than alcohol (wine) because cold water strengthens the nerves¹.

Galen (125-200 A.D.) described the etiology, classification and management of *Ra'asha* in detail. He mentions that the basic cause of *Ra'asha* is weakness of various faculties (*Quwa*) of the body. It is because of this reason that it mostly occurs because of excessive elimination (*Kasrat-e-Istiferagh*), excessive fatigue, starvation and excessive indulgence in sex. Sometimes it may occur because of the humoral excess (*Kasrat-e-akhlal*) as they produce a burden on the faculties of the body¹.

While elaborating on the etiology of *Ra'asha*, Galen asserts that this disease is more severe in old age persons and it may occur in them consequent to the relatively less severe factors. On the contrary *Ra'asha* occurs in young adults only when there is extreme coldness (*Buroodat*) in their body. Various other causes of *Ra'asha* include excessive consumption of alcohol, chronic diarrhoea, excessive eating with no physical activity etc. All these factors produce derangement in temperament resulting in excessive coldness in the body (*Sui Mizaj Barid*). Sometimes viscid humours may obstruct the pathways of *Rooh-e-Nafsani* and result in *Ra'asha*¹.

Symptoms of Parkinson's disease were described by the Greek physician Galen (129-200 A.D.) who worked in ancient Rome. He wrote of tremors of the hand at rest¹⁸. He wrote extensively on disorders of motor function, including the book on tremor, palpitation, convulsion and shivering. He distinguished between forms of shaking of the limbs on the basis of origin and appearance. The aged, he noted, exhibited tremor because of decline in their power to control motion of their limbs. The key to overcoming tremor was to abolish the proximal cause but for the aged, this was impractical. He related that a person suffering from "catoche" has wild, wide open eyes (Reptilian stare) due to lid retraction², that he lies rigid in bed, as if he were made of wood. He also suffers from tremor, constipation and certain psychiatric symptoms.

Apart from Roofus and Galen other scholars of Roman era have also discussed *Ra'asha*, the most notable among them being Pythagoras (4th and 5th A.D.)¹.

The Unani system of medicine was transferred to Arabian Peninsula after the fall of Roman Empire. Hunain-ibn Masaviya (777-857 A.D.) was the first Arab scholar to discuss this disease. He mentions that Castorium (*Jund-badaster*) 3-4 gms given with warm water is very beneficial in *Ra'asha*. Piper (*Filfil*) is also very useful in this disease¹.

Ali ibn Rabban al-Tabari (810 A.D.) is one of the famous scholars of this period and he has given ample space to *Ra'asha* in his book *Firdousal Hikmat*. He asserted that *Ra'asha* occurs because of excessive consumption of cold water and alcohol particularly when consumed on full stomach. Having sexual intercourse in inebriated condition is also one of its causes. Castorium (*Jund-badaster*), Asafoetida (*Hilteet*) and *Roghan-e-gust* are useful in this disease^{1,3}.

The famous physician and intellectual of Islamic era, Abu Baker Mohammad ibn Zakaria al-Razi (865-925 A.D.) has described *Ra'asha* under the context of diseases of head in the first part of his famous treatise *Al Hawi Fi al-Tib*. While he has quoted various assertions of the scholars of Greek and Roman eras, he has also mentioned the various etiological factors and the management of *Ra'asha* in certain detail. Some of his assertions are listed below:

"*Ra'asha* occurs because of the weakness of nerves. Sometimes it may occur because of excessive consumption of cold water and alcohol particularly during fever. If any external factor is responsible for causation of *Ra'asha*, the patient should be prevented from getting exposed to it. If the condition persists, *Roghan-e-Kasual Himar* should be used locally on the part"¹.

There is one full chapter on *Ra'asha* in *Mo'alejat-e-Buqratia* written by Ahmad ibn Mohammad al-Tabari (d. 985 A.D.). He has classified *Ra'asha* into three main types according to the different causes and has discussed their management as well⁴.

Ali ibn Abbas al-Majoosi (930-996 A.D.), the author of *Kamil-us-Sana'a*, asserts that *Ra'asha* is caused by the weakness of motor functions of that particular organ which exhibits tremors. This weakness may result either from intrinsic or extrinsic factors. The intrinsic factors include excessive consumption of cold water and alcohol, general weakness of the old age or the presence of viscid humors in the path ways of motor activity. All these factors result in the weakness in the activity of the organ involved⁵.

Avicenna (980-1037 A.D.), the author of famous book *Al Qanoon Fil Tib* has described *Ra'asha* as a disease of organs produced because of weakness in motor activity to such extent that it cannot overcome the resting force applied by mass of the organ (*Suful-e-'Azo*). He has also described the etiology, the clinical manifestations and management of *Ra'asha* in detail. He has asserted that the basic factor responsible for *Ra'asha* is the weakness in motor activity of the organ¹.

Avicenna (980-1037 A.D.), the Persian polymath and foremost physician of his time discussed the various forms of motor unrest in his chapter on nervous disorders in the *Canon of Medicine*. The description of tremor is not unexpectedly similar to that of Galen, as it was based on previous works including that of Galen. A range of measures are proposed according to the cause of the disorder. Bathing in sea-water or in mineral baths (nitrate, arsenic, asphalt, sulphur) was recommended, as was the ever popular evacuation; composite preparations including made from the excretion of the anal gland of the beaver (*Oleum castoreum*) – a common spasmolytic – mixed with honey and cold oil, to which pills formed from rue (*Ruta graveolens*) and scolopendrium (*Scolopendrium vulgare*; hart's tongue).

Sheikh Ismail Jurjani (d. 1140 A.D.) in *Zakhira-e-Khwarazm Shahi* defined *Ra'asha* as the trembling of organs. He has further asserted that it occurs only in voluntary organs and is manifested by involuntary movements. He has classified its causes into three main types:

- The weakness of motor activity (*Zouf-e-Quwat-e-Muharrika*).
- The weakness of the organ involved (*Zouf-e-Aalai Harkat*).
- A combination of the above two⁶.

Other scholars of Arabic era like Qusta ibn Lauqa¹, Sabit ibn-e-Qurrah⁷, Nooh ibn Mansoor al-Qamari⁸ and Abu Marwan Abdul Malik ibn Zuhr⁹, have also discussed *Ra'asha* in their respective texts but have not added much to what was described by their predecessors.

The scholars of Indian subcontinent also recognized this disease and all of them have discussed it. Some of the renowned scholars of this period include Hakim Mohammed Akbar Arzani¹⁰, Hakim Shareef Khan¹¹, Hakim Ajmal Khan¹², Hakim Mohammed Azam Khan²⁴, Hakim Ghulam Jeelani¹³ and Hakim Mohammed Kabiruddin¹⁴. But none of them has added to the already existing literature.

In Ayurveda, description of the symptoms of Parkinson's disease is found, which they called *Kampavata* (5000 B.C.). To treat *Kampavata*, they used a tropical legume called *Mucuna pruriens* (*Konch*), which they called *Atmagupta*. The seeds of *Mucuna pruriens* are a natural source of therapeutic quantities of L-dopa¹⁵. *Mucuna pruriens* is certainly the oldest known method of treating the symptoms of Parkinson's disease, and is still being used to treat Parkinson's disease.

The first formal description of Parkinson's disease was first formally described in modern times in *An Essay on the Shaking Palsy*¹⁶, published in 1817 by a London physician named James Parkinson (1755-1824)^{17,18}. James Parkinson systematically described the medical history of six individuals who had symptoms of the disease that eventually bore his name. Unusually for such a description, he did not actually examine all these patients himself but observed them on daily walks. The purpose of his essay was to document the symptoms of the disorder, which he described as "Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards and to pass from a walking to a running pace: the senses and intellect being uninjured."

Nomenclature of Parkinson's disease: It was not until 1861 and 1862 that Jean-Martin Charcot (1825-1893)^{25,26} with Alfred Vulpian (1826-1887) added more symptoms to James Parkinson's clinical description (Charcot and Vulpian, 1861, 1862) and then subsequently confirmed James Parkinson's place in medical history by attaching the name Parkinson's disease to the syndrome. Charcot added to the list of symptoms the mask face, various forms of contractions of hands and feet, akathisia as well as rigidity. It was quite difficult to understand from his description what was meant by referring to rigidity. It was only after Charcot gave a clinical lesson in 1868 that the difference became clear (Charcot, 1868). In 1867 Charcot introduced a treatment with the alkaloid drug Hyoscine (Scopolamine) derived from the Datura plant, which was used until the advent of levodopa (L-Dopa) a century later. In 1876 Charcot described a patient suffering from Parkinson's disease in the absence of tremor, while rigidity was present. In this case

there was no paralysis, so Charcot rejected the term “Paralysis Agitans”. Instead he suggested that the disease be referred to in future as Parkinson’s disease.

The publication was entitled *An Essay on the Shaking Palsy*. This established Parkinson’s disease as a recognized medical condition. The essay was intended to encourage others to study the disease. Some 60 years after it was first published, a French neurologist by the name of Jean Martin Charcot did exactly that, Charcot was the first to truly recognize the importance of Parkinson’s work and named the disease after him. Much has been learned about the disease yet much remains a mystery. The symptoms are progressive and degenerative and tend to be more common in older individuals. It is understood that a dopamine deficiency in the brain is at the root of the matter, yet why this initially occurs is less clear.

It was in the 1960s that the chemical differences in the brains of Parkinson’s patients were identified. The low levels of dopamine cause the degeneration of nerve cells in part of the brain called the substantia nigra. It was this discovery that led to the first effective medicinal treatment of the disease. In the 1960’s the drug Levodopa was first administered to treat the symptoms and has since become the “gold standard” in medication.

Since the 1960’s research has continued to progress at a rapid rate. Despite the fact there is still no cure, the symptoms can now be effectively controlled and reduced in severity. The Parkinson’s Disease Foundation was established in America in 1957 to assist sufferers and to fund and promote further research. Many other foundations assisting the cause have been established in the following years. A notable recent addition is the Michael J. Fox Foundation, named after the much loved television and movie actor. The foundation has been very public about its goal of developing a cure for the disease within this decade. Since its inception in 2000 it has succeeded in raising over 90 million US dollars. The nineteenth century witnessed a revolution in the science and technology. The medicine also shared its benefits which resulted in the better understanding of the disease and helped in unveiling the mysteries associated with pathogenesis, the etiology and the management of various diseases. *Ra’asha* which was described as a disease for centuries was recognized and established as a clinical feature of a number of diseases. The first major development in this direction was put forward in 1817 by James Parkinson who wrote an essay on “The shaking palsy” in which he described what is now known as Parkinson’s disease. He coined the term “paralysis agitans” for the idiopathic parkinsonism². Although the clinical features of this disease were recognized, yet its etiology and pathology remained obscure up to the end of nineteenth century A.D. In early twentieth century small epidemics of a new mysterious disease broke out around the world. This disease was later on described for the first time by Von Economo. The acute phase of this disease was known as “Encephalitis Lethargica” while as its chronic phase was originally called chronic encephalitis which was later named as Parkinsonism.

In 1960 A.D. Henry Kiewicz discovered that Parkinson’s disease was caused by dopamine deficiency in substantia nigra of the brain. In the normal brain melanin containing pigmented neurons in the pars compacta of substantia nigra is responsible for motor activity. Evidence suggests that the death of the dopaminergic neurons begin a decade before symptoms onset. When the neuronal loss reaches about 70% of the total neurons, symptoms begin which are given below^{19,2}:

- Tremor or trembling in hands, arms, leg, jaw and face.
- Rigidity or stiffness of limbs, and trunk.
- Bradykinesia or diminished speed and spontaneity of voluntary movement.
- Postural instability or impaired balance and co-ordination.

In 1983 A.D. this disease was seen in humans in San Francisco who were exposed to Methyl Phenyl tetrahydroprophyridine manganese (MPTP)²⁰.

Biochemistry of L-dopa: The underlying biochemical changes in the brain were identified in the 1950s due to largely the work of Swedish Scientist Arvid Carlsson (b. 1923). In the 1950’s, Arvid Carlsson demonstrated that dopamine was a neurotransmitter in the brain and not just a precursor for norepinephrine, as had been previously believed. He developed a method for measuring the amount of dopamine in brain tissues and found that dopamine levels in the basal ganglia, a brain area important for movement, were particularly high. He then showed that giving animals the drug reserpine caused a decrease in dopamine levels and a loss of movement control. These effects were similar to the symptoms of Parkinson’s disease. Arvid Carlsson subsequently won the Nobel Prize in Physiology or Medicine in 2000 along with co-recipients Eric Kandel and Paul Greengard²¹.

Therapeutic use of L-dopa: These findings led other doctors to try of L-Dopa with human Parkinson's patients and found it to alleviate some of the symptoms in the early stages of Parkinson's. Unlike dopamine, its precursor L-Dopa could pass the blood brain barrier. The validity of the approach was shown by the transient benefit seen after injection of L-dopa. However, it was not of practical value as a treatment because of the severe toxicity associated with the injection. At this point, George C. Cotzias (1918-1977) made a critical observation that converted the transient response into a successful, large scale treatment²³. By starting with very small doses of DOPA, given orally every two hours under continued observation and gradually increasing the dose he was able to stabilize patients on large enough doses to cause a dramatic remission of their symptoms. The first study reporting improvements in patients with Parkinson's disease resulting from treatment with L-dopa was published in 1968²². The result was soon confirmed by other investigators and has now become the standard treatment for Parkinsonian symptoms.

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