

# The chronic residual respiratory disorder in post-encephalitic Parkinsonism

ROBERT KIM

*From the Neurological Unit of the Boston City Hospital and Department of Neurology, Harvard Medical School, Boston, Massachusetts, U.S.A.*

Respiratory disorders were a prominent feature of the acute phase in many outbreaks of epidemic lethargic encephalitis in 1918-25. They occurred both in the acute stages of the illness and as sequelae. They were reported in conjunction with all the other common manifestations of the residual post-encephalitic symptoms and occasionally were the only manifestations of the syndrome. Many of the disorders in early stages of the disease were complex, compulsive tics such as reported by Babinski and Charpentier (1922). One of their patients had an episodic disorder occurring more frequently in the evening and consisting of contraction of the nares followed by slow respirations, as low as six per minute, then interruption of respiration in the inspiratory position and finally prolonged snorting respiration through the nose as if trying to dislodge a nasal plug. It was noted that the patient could exercise some control over the disorder but could not stop it completely. The tic-like nature of the phenomenon at first led some to the conclusion that it was hysterical, though its association with the other compulsive manifestations of the disease and the occurrence of many other similar cases in post-encephalitic patients disproved this assumption.

By the time Turner and Critchley (1925) wrote their paper on respiratory disorders in epidemic encephalitis there had been many case reports of similar complex compulsive disorders in respiration. These authors present a good review of the French and English literature to that time. Respiratory disorders were classified into the following categories:

1. *Disorders of respiratory rate* Tachypnoea was the most common disorder and was noted to be either continuous or episodic. It could occur at any time, sleeping or awake, with rates as high as 100 per minute. Slow breathing was less common.
2. *Dysrhythmias or disorders of the respiratory rhythm* Among these were included Cheyne-Stokes respiration (rare), breath-holding spells, sighs, forced or noisy expiration, and the inversion of the inspiration-expiration ratio.

3. *Respiratory tics* These included yawning, hic-cough, spasmodic cough, and sniffing.

Though reporting only the more dramatic disorders, Turner and Critchley (1925) pointed out that slighter dysrhythmias were not uncommon.

Jelliffe's monograph (1927) contains a complete historical review, and reports two further cases with psychopathological studies.

Of the many respiratory disorders reported, perhaps the most dramatic were observed by Wolff and Lennox (1928). The episodes they observed would begin with increasing hyperpnoea leading to apnoea. During the hyperpnoeic phase, the face took on a look of anxiety and there was an increasing taughness of muscles with twisting and turning of the body. During the apnoeic phase, the patient turned cyanotic and then fell unconscious, and finally had a grand-mal seizure. The authors considered the possibility that the whole sequence was a manifestation of seizure disorder but concluded that the syncope was due to apnoea and a Valsalva's manoeuvre and that the seizure was secondary to hypoxia.

Since the 1920s there have been few reports. Nugent, Harris, Cohn, Smith, and Tyler (1958) noted decreased maximum breathing capacity and dyspnoea in 50% of Parkinsonian patients. These authors felt this was due to rigidity of chest wall muscles and noted that exertion could increase the maximum breathing capacity beyond the volitional ability to do so. Recently, De La Torre, Mier, and Boshes (1960) mentioned irregularity of respiration in Parkinsonian patients and confirmed an incidence of 50% of Parkinsonians with reduced breathing capacity. Grewel (1957) quotes a paper by Schilling in the German literature which characterizes Parkinsonian 'vegetative' respiration as lacking in the natural undulations and as being wider and more irregular. Grewel reviewed the speech disorders in Parkinsonism but stressed disturbance of facial and lingual and pharyngo-laryngeal muscles.

Schmidt and Kaniak (1960) noted that many of

their patients with stereotaxic lesions (site of ablations not mentioned) developed pulmonary complications. They noted reduction in respiratory performance, especially in the ability to cough and to breathe deeply. Petit and Delhez (1961) studied diaphragm and intercostal muscles with the electromyogram and report, in Parkinsonian patients, that diaphragmatic muscles appear normal or near normal, while intercostal muscles showed constant discharge through inspiration and expiration and it was thought that this interfered with respiratory function. Only when the patient was extremely anxious did the diaphragm show continuous discharge.

Descriptions of respiratory disorders of the post-encephalitic syndrome have dealt almost exclusively with episodic phenomena occurring within several years of the time of lethargic encephalitis. The respiratory status in patients with long-standing disease has received little attention. The present study was undertaken to characterize resting respiration in the long-term post-encephalitic Parkinsonian patient. A previously unreported disorder of voluntary control of automatic respiratory functions is noted.

#### METHOD

Nine patients with Parkinsonism were studied. Four of these patients (M.H., N.T., M.W., L.C.) had all of the following features; a history of influenza between 1918-25, early onset of the Parkinsonian syndrome between the ages of 16-40, with well-documented oculogyric crises. One patient, M.S., had a history of influenza, onset of illness before the age of 50 and, in addition to the usual features of Parkinsonism, she had anisocoria and unreactive pupils. The mother of the sixth patient (J.H.) had influenza during the seventh month of gestation and his Parkinsonian symptoms started at the age of 22. J.G. had a history of influenza during the first world war and had onset of Parkinsonism at the age of 55. All of these seven patients have been fully evaluated as in-patients of the Neurological Unit of the Boston City Hospital or related chronic service of the Long Island Hospital. Of the two remaining patients, D.S. had influenza in 1916 and developed Parkinsonism in 1956, and J.M. the last, had no history of influenza, onset at the age of 45, and all signs of Parkinsonism are minimal.

The apparatus consisted of an ink-recording respirometer. A mask rather than a mouthpiece was used, so that subjects could speak during the tests and so that bucco-facial and lingual motions would be left intact. A soda-lime carbon dioxide absorber was used and oxygen was fed into the system so that recordings could be taken over long periods (up to one hour without interruption). Breathing in this apparatus was not distressing and early anxiety rapidly subsided. Readings of resting respirations were taken as well as some simple

tasks such as breath-holding, singing, speaking, and reciting the Lord's Prayer with as few breaths as possible. Subjects were asked to cough voluntarily and the reaction to spirits of ammonia introduced into the system was tested. At the same time that the respirometer recorded airflow, an abdominal cuff recorded expansion and contraction of chest and abdominal motion. In this way muscular motions of breathing could be correlated with airflow.

#### RESULTS

**1. RESTING RESPIRATION Rate** All Parkinsonian patients had rapid respiratory rates compared with controls. The rates of normal individuals ranged from eight to 13 respirations per minute and averaged 11, while patients with post-encephalitic Parkinsonism ranged from 13 to 31 and averaged 19 (Figs. 1a and b) (Table I).

**Regularity of amplitude of respiration** In those subjects in whom a two-minute consecutive period of respiration uninterrupted by signs or disorders of respiratory rhythm could be measured, it was found that Parkinsonian patients had more regular respirations than controls. This would reflect the absence of regular undulations seen in normal

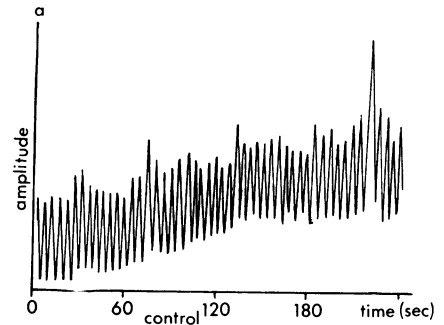


FIG. 1a. An example of normal respiration in a 21-year-old woman. There is considerable variation in amplitude of respiration, which occurs in undulations.

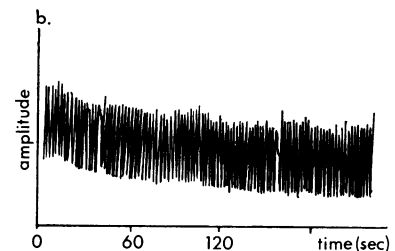


FIG. 1b. An example of post-encephalitic respiration. Respirations are rapid with reduced variation in amplitude and there are two pauses.

TABLE I  
RESPIRATORY RATE<sup>1</sup>

Post-encephalitics		Controls	
patient	resp./min.	patient	resp./min.
J.G.	22	T.J.	10
M.H.	20	H.K.	13
J.H.	16	E.O.	8
N.T.	20	P.G.	13
M.W.	31	H.F.	9
D.S.	18.5	J.R.	13
M.S.	16		
J.M.	13	Average	11
L.C.	16	Spread	8-13
Average	19		
Spread	13-31		

<sup>1</sup> Post-encephalitic patients showed increased respiratory rate.

respirations. To arrive at a numerical measurement of variability of respiration the '% average deviation from the mean breath amplitude'<sup>1</sup> was used. This is a measure of regularity of respiration corrected for basic amplitude (see Figs. 1a and b) (Table II). It was interesting to note that one patient, M.S., who had three separate recording sessions, showed extremely irregular resting respirations interrupted by frequent pauses in respiration during two of the sessions (Fig. 2a), but on the third session the respirations were regular and showed a lack of variability in amplitude (Fig. 2b). In M.H., the % deviation (21.4) was high for both patients and controls but the basic amplitude was so low that it tended to amplify the size of the deviation and may well have represented a leak about the mask. J.M. was excluded from these measurements because of inability to find two minutes respiration uninterrupted by signs—that is, breaths three times basic amplitude or larger. The average % deviation from the mean for controls was 12.3% with a spread of 9.8% to 14.2%. The average % deviation from the mean among post-encephalitics was 8.6% with a spread of 4.3% to 21.4%. If the figure from M.H. is omitted the average among post-encephalitic patients drops to 5.6% and the spread drops to an upper level of 11.6%. These tracings indicate that the decreased variability of respiration among Parkinsonian patients, though striking, is inconstant. In some the variability is actually increased but in many this results from irregularities of rhythm in respiration.

<sup>1</sup> To arrive at a measurement of variability of respiratory amplitude, the amplitude of respiration was measured for two minutes of consecutive breathing. These amplitudes were averaged to give a mean breath amplitude. Each breath's amplitude was then subtracted from the mean breath amplitude to give a deviation from the mean amplitude. This deviation from the mean amplitude of each breath was averaged to give an average deviation from the mean breath amplitude and this was expressed as the per cent of average deviation from the mean breath amplitude.

TABLE II  
REGULARITY OF RESPIRATION<sup>1</sup>

Patient	Mean amplitude (mm)	Per cent deviation from mean
<i>Post-encephalitics</i>		
J.G.	25.0	11.6
M.H. <sup>2</sup>	7.8	21.4
J.H.	15.5	4.7
N.T.	25.5	5.7
M.W.	23.3	4.3
D.S.	20.5	7.7
M.S.	27.4	5.0
Average		8.6
<i>Controls</i>		
T.J.	27.5	13.4
H.K.	22.3	9.8
E.O.	19.7	14.2
P.G.	29.1	13.4
H.F.	45.5	11.8
J.R.	28.8	11.4
Average		12.3

<sup>1</sup> The per cent deviation of amplitude from the mean is a measure of the regularity of respiration corrected for base amplitude. Parkinsonian patients had low per cent deviation from the mean breath amplitude indicating more regular respiration.

<sup>2</sup> The low mean amplitude in M.H. indicates there may have been a leak in the system and thus increased the per cent deviation from the mean. If this value is dropped the average drops to 5.6% among post-encephalitic patients.

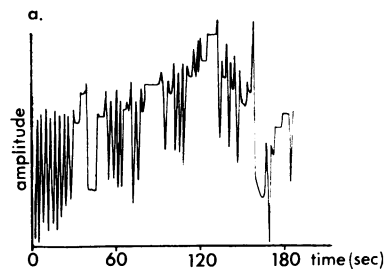


FIG. 2a. An example of markedly irregular respiration in a post-encephalitic Parkinsonian patient. There are multiple involuntary pauses after a short regular interval.

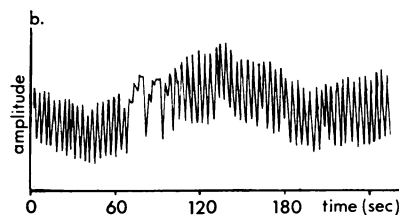


FIG. 2b. From the same patient as in Fig. 2a, now showing more regular respiration with, however, occasional pauses.

## 2. ABILITY TO MODULATE AUTOMATIC RESPIRATION

All but one of the patients, J.M., in this series showed a loss, to a variable degree, of ability to alter automatic respiratory rhythm in order to perform speech or some other task. Most striking in this respect was the inability of the Parkinsonian patient to hold a breath (Figs. 3a and b). This inability varied from marked and constant in M.W. to mild and inconstant in others. In one patient, M.S. (Fig. 3c), it was interesting to note that, while she was able to hold the respiratory kymograph steady (probably by closing her glottis), the abdominal tracings revealed rhythmic respiratory motions. This patient was remarkable in that she had marked involuntary motions of her tongue and jaw. At rest her tongue would be protruded out and down and would often dart back into her mouth while the jaw performed masticating motions. This patient had markedly irregular respirations on two out of three recording sessions.

A similar disorder occurred when patients attempted to recite the Lord's Prayer in one breath. While controls were able to do this without difficulty, patients with Parkinsonism had to take numerous breaths to complete the task (Fig. 4a). In one case, J.G., the patient was able to avoid any deep inspiration but abdominal recordings showed continued respiratory motions during his even recital (Fig. 4b). It is interesting that this patient was able to dissociate a rhythmic portion of respiratory motion which could affect a constant outflow of air usable in smooth speech. That this represents a dissociation of diaphragmatic from intercostal or accessory muscle function is not clear from this study.

### 3. RESPIRATORY IRREGULARITIES

While all controls were free of any unusual interruption of respiration, five of the eight patients showed some episodic disturbance. Most common was a simple lapse in the smooth respiratory curve and it occurred in both inspiration and expiration (Figs. 1b, 2a and 2b). The frequency of these respiratory lapses varied both from patient to patient and from time to time in the same patient. No patient was aware of these lapses or pauses.

There were none of the more dramatic respiratory episodes described in the literature of the 1920s.

### 4. COUGH

Evaluating cough in terms of both sensitivity and efficiency was difficult. The chest wall in Parkinsonian patients appeared more rigid and often cough seemed weak but our recorder was not designed to measure such differences. In terms of ease of eliciting cough, spirits of ammonia seemed to work as well in Parkinsonians as in controls.

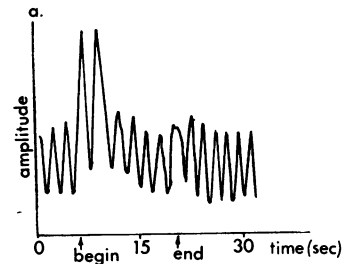


FIG. 3a. To illustrate total inability to hold breath in a patient with post-encephalitic Parkinsonism. The patient tried again and again to do this task but was never able to do any better.

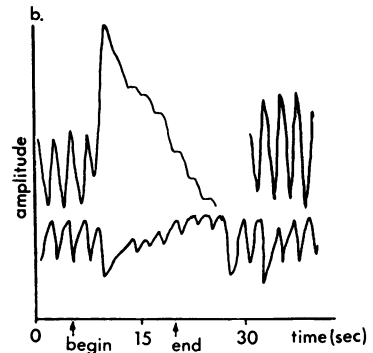


FIG. 3b. This tracing illustrates inability to hold breath but not as severe as in Fig. 3a. Respiratory undulations appear in modified form in both airflow (upper) and abdominal cuff (lower) tracings.

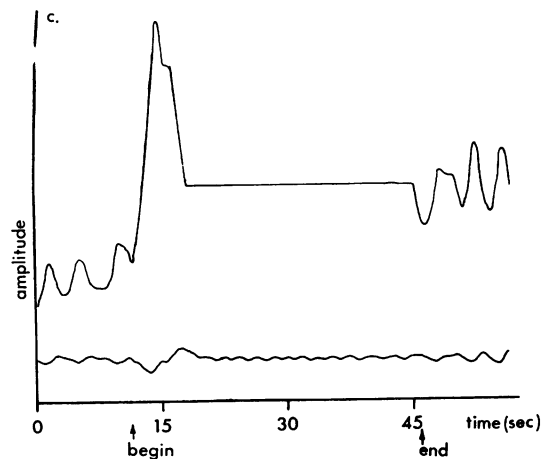


FIG. 3c. Almost complete ability to hold breath but the abdominal cuff tracing (lower) shows continued rhythmical respiratory motion. Airflow arrest was probably accomplished by closure at the glottis or pharynx. Normal people can hold both airflow and abdominal tracings level.

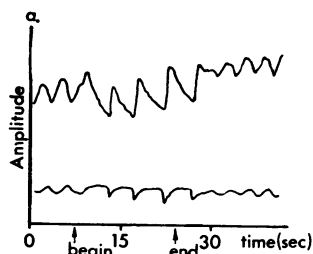


FIG. 4a. In this tracing a post-encephalitic subject attempts to recite the Lord's Prayer in one breath. Recitations were hurried, poorly articulated, and interrupted by many breaths. Normal individuals can recite the Lord's Prayer in one breath.

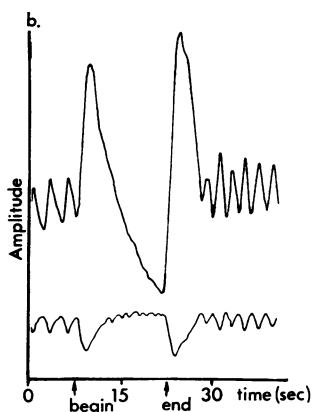


FIG. 4b. A post-encephalitic patient successfully recites the Lord's Prayer in one breath but the abdominal cuff tracing (lower) reveals continued respiratory motion. Normal individuals are able to keep both curves smooth.

#### DISCUSSION

In this study the most common respiratory disorder was an increase in respiratory rate. This finding agrees well with previous studies. Also noted was an increased regularity of respiration. The respiration of Parkinsonian patients was quite level and free of wave-like increases and decreases in depth of respiration. The lack of natural undulations in respiratory amplitude may be due to some limitation of movement by chest wall rigidity or to a relative insensitivity to stimuli from the periphery which might govern small corrections. It is unlikely that chemoreceptor stimulation is changed in this disease, and, when increased levels of  $\text{CO}_2$  were allowed to accumulate in the system by cutting out the soda lime absorber, both post-encephalitics

and controls responded with increased depth and to a less degree increased frequency of respiration. No difference in response between the two was seen. The role of proprioceptive stimuli in control of respiration is not clear. It should be noted that most previous observations on abnormal respiration were made during episodic disorders. The observations in this paper occurred during the usual (for each patient) breathing and no patient was aware of any abnormality or discomfort in breathing.

The most striking disorder we have found is the difficulty in inhibiting respiratory rhythm in performance of other effort. All but one patient showed some degree of this difficulty and in two it was absolute. This indicates a degree of loss of higher control of the automatic reflex respiratory mechanism that parallels the loss or restriction of other willed movement in this disease. The locus caeruleus is considered to be a pneumotoxic centre (Oberholzer and Tofani, 1960) and changes in this nucleus have been reported in both acute (Klarfeld, 1922; Meyer, 1923; Holzer, 1926)—and chronic (Greenfield and Bosanquet, 1953)—post-encephalitic states. Destruction of the locus caeruleus in man leads to severe cerebral dyspnoea with emphasis on the inspiratory phase of respiration or to periodic respiration (Hess and Pollack, 1924). This is not the disorder observed in this paper. Some additional lesion must therefore be present. Structures at midbrain level are also important in the control of respiration (Oberholzer and Tofani, 1960), and Economo (1931) made cogent argument for high level control of respiration by the substantia nigra, which is also severely affected in this disease, discussed by Denny-Brown (1962).

Though little is known of the purposive control of respiration by extra-pyramidal pathways, we wish to draw attention to a very characteristic interference with higher levels of respiratory adaptation associated with mesencephalic disorder in post-encephalitic Parkinsonism.

#### SUMMARY

Respiration in post-encephalitic Parkinsonism was studied. Tracings on a respirometer revealed that during the resting state post-encephalitic patients have more rapid respirations with fewer variations in amplitude than normal controls. This had been previously described but usually occurred in episodic form. The most striking finding was decreased ability to interrupt automatic aspects of respiration by volitional control as demonstrated by inability to hold breath.

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