

A STUDY OF RESPIRATION AND CIRCULATION IN EPILEPSY *

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Modern methods of study have already assisted in the explanation of many of the physiological facts bearing on circulation and respiration, and have explained the pathogenesis of many of the disorders of these systems.

An analysis of the clinical features of epilepsy reveals a vague and unsatisfactory description of the symptoms referable to the circulatory and respiratory systems.

A study of some of the circulatory and respiratory disturbances of epilepsy by modern methods of investigation was therefore considered important.

This report is based on the results obtained from the examination of forty-four cases. All of these cases were examined on two, some three and four and a few up to fifteen different occasions.

The examination included a graphic study of the heart action, employing tracings of the jugular and brachial pulses and the apex beat. Blood-pressure estimations and continuous blood-pressure and respiratory curves were made. There were 225 tracings obtained from the forty-four patients.

The tracings were obtained by means of the Erlanger sphygmomanometer with a Hirschfelder attachment, and an Ellis pneumograph.

This report is not as extensive as we could wish, nor the evidence as voluminous as it should be. The difficulty of obtaining a continuous blood-pressure curve on a patient during a convulsion is self-evident. The obtaining of a tracing which includes the time preceding and following the convulsion is largely a matter of luck and many tracings may be made before one is successful.

The association of epilepsy with heart disease has been observed for many years. This association may be the result of several factors. First, the heart disease may be accidental. Second, the epilepsy may be responsible for the cardiac changes, and, third, the cardiovascular change may be responsible for the epilepsy. The third group is a small one and

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includes the late or tardy epilepsies. This condition having no bearing on our findings, will not be discussed. It is, however, fitting to call attention to the so-called epileptic convulsions accompanied by stoppage of the heart, bradycardia or other arrhythmia.

Bradycardia has been noted by Seguin (21-24) Corkey and Hubberty (11-76), Drummond (5-15), Gibbings (12) and many others. In the light of our present knowledge of heart-block it is extremely probable that it was this condition which the above authorities observed.

Stoppage of the heart (?) has been observed by Moxon and Tagge and Smith while auscultating the heart. Failure of the pulse has been observed by Hughlings Jackson and Russel. Whether these cases were heart-block or hemisystole cannot be said, for lack of graphic records. Munson¹ did not find a single case of stoppage of the heart in epilepsy, employing graphic methods as a means of study.

There are found in the literature numerous references to the abnormal condition of the heart in epilepsy. Valvular lesions, hypertrophy and arrhythmias have been frequently noted.

Browning,² after examining 150 cases, states that normal sounds and a normally acting heart are the exception rather than the rule.

Of the forty-four cases examined by us, thirty-five showed an abnormal condition of the heart; of these, ten showed gross lesions and twenty-five a functional change manifested by hemic murmurs, abnormality of sound and sinus arrhythmia. Valvular lesions were observed four times. Hypertrophy was observed seven times. Diastolic irregularity was observed twelve times. Abnormal sounds were observed thirteen times. Hemic murmurs were observed four times. Heart block was observed once. Irritable heart was observed once. Nodal rhythm was observed once. Auricular extrasystoles were observed once. The case of heart-block exhibited true epilepsy and not the syncopal attacks of the Stokes-Adams syndrome. Although it is generally agreed that sinus arrhythmia is of vagal origin, no relation between it and the Traube-Hering waves (to be described later) was observed. Hypertrophy of the heart occurred in patients in middle life or above, with two exceptions.

BLOOD-PRESSURE

Owing to the diversity of methods employed by the numerous investigators, and the mechanical defects of many of their instruments, the work of the older authors, such as Feré, must be discounted. Of the more recent investigations it may likewise be said that the methods differ, that the observations have been too limited in number, and that graphic methods allowing of the study of continuous blood-pressure

1. Munson: *Jour. Am. Med. Assn.*, 1908, 1, 681.

2. Browning, Wm.: *Jour. Nerv. and Ment. Dis.*, 1893, xviii.

curves have not been utilized. It is apparent that one cannot detect a change in blood-pressure occurring within the space of several seconds by the use of such instruments as the Riva-Rocci, Janeway, Stanton, etc.

Summed up, the results of the more recent investigations are as follows: There is a high blood-pressure during the convulsion; the blood-pressure falls rapidly after the convulsion, but remains higher than normal between convulsions. (Plaskuda, Morgenthaler, Fleury, L'Alle-mant and Rodiet and others.)

Our results will be tabulated under the following headings. 1. General blood-pressure. 2. Respiratory change in blood-pressure. 3. Traube-Hering waves. 4. Changes relative to the convulsion.

1. Of 41 cases examined as to general blood-pressure, 18 had a systolic blood-pressure of 120 or below, and 23 above 125 ranging to 200. Of 17 cases examined on the day of a convulsion, seven had a systolic blood-pressure above 135, and 10 were below 120.

The pulse-pressure, estimated by the difference between the systolic and diastolic pressures, was 50 or above in 21 cases, 40 or above in 15 cases and 45 in 5 cases. Of 8 cases showing a pulse-pressure above 55, 5 were either measured on the day of a convulsion or had some cardio-vascular disease.

Owing to the paucity of material, and taking into consideration the individual variations, variations of emotion, sensory stimuli, etc., no hard and fast conclusions can be made from this particular part of the work. The systolic blood-pressure and pulse-pressure were higher than normal in a little more than one-half the cases; the pulse-pressure was below normal in many. The cases showing cardiovascular disease had high pulse-pressure. The cases showing high systolic blood-pressure on the day of a convulsion likewise showed a high pulse-pressure.

2. Respiratory change in blood-pressure: In 21 cases showing respiratory changes in blood-pressure our results bear out Erlanger and Festerling's³ findings. The arterial pressure falls during inspiration and rises during expiration. During the labored breathing following a convulsion, the respiratory changes in blood-pressure are very marked.

3. Traube-Hering waves: Under certain unusual conditions, there are found in addition to the respiratory rhythmical falls and rises of blood-pressure, changes in blood-pressure, the waves of which are much larger than those due to respiratory movements. These waves were first described by Traube.⁴ Hering⁵ considered them as arising as a result of irradiation from the respiratory center. Horatio Wood, Jr.,⁶ in a

3. Erlanger, Joseph, and Festerling, E. G.: *Jour. Exper. Med.*, 1912, xv, No. 4, p. 37.

4. Traube: *Centralbl. f. d. Med. Wissensch.*, 1865, p. 1881.

5. Hering: Quoted by Horatio Wood, Jr. (see note 6).

6. Wood, Horatio, Jr.: *Am. Jour. Physiol.*, 1899, No. 2, p. 352.

study on the origin of Traube waves, comes to the conclusion that they do not arise in the respiratory center. He was able to paralyze the respiratory center through the action of veratrin, the vasomotor center remaining intact. Under these conditions he was still able to observe Traube waves (Fig. 1).

The ultimate cause of these waves is not well understood, but they are probably due to a rhythmical activity of the vasomotor center. Although a rhythmical activity of the vasoconstrictor center is said to be present throughout life, there are no definite data relative to the occurrence of these waves in man.

They have often been observed during experiments on animals, especially in experiments increasing the intracranial tension. They have likewise, occasionally, been observed in apparently normal human subjects. However, although present at times, they are the exception rather

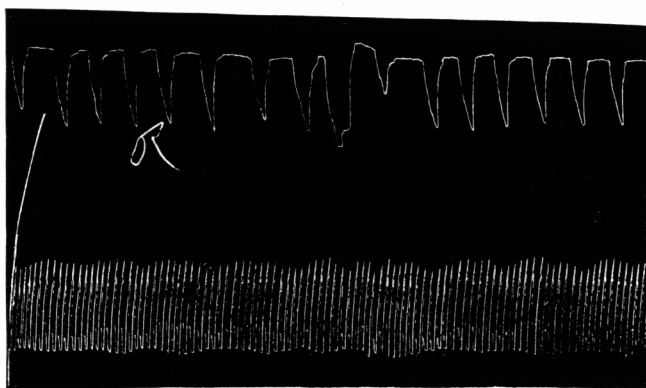


Fig. 1.—Traube-Hering waves not due to respiratory change. Upper tracing, respiration; lower, blood-pressure.

than the rule. Many other waves of change in blood-pressure may be observed in man and should be definitely differentiated from the Traube-Hering waves. Emotion, muscular movement, peripheral stimulation, etc., all produce change in the continuous blood-pressure tracings. Changes due to muscular movements can easily be differentiated, as pointed out by Erlanger;³ those due to emotion, etc., are not rhythmical and do not have a gradually increasing and diminishing size. In the interpretations of our tracings the following conditions were insisted on before Traube-Hering waves were said to be present. 1. The column of mercury in the manometer had sunk to its lowest level after inflating the arm-band before the drum was started. 2. All muscular movements were carefully watched for, and marked as such on the drum. 3. All waves due to emotion and other causes were excluded. 4. Following the convulsion the column of mercury was at the same level as before it. The

waves will be described relative to their occurrence, length and relation to pulse change.

Of the 44 cases, 24 showed the presence of Traube-Hering waves. Of 15 cases examined on the same day as the convulsion, 7 showed marked waves, 6 moderate waves and 2 no waves.

Of 14 cases examined within five days after a convulsion, 3 showed marked waves, in 7 waves were present and 4 showed no waves.

Of 15 cases examined more than five days after, one showed moderate waves twenty days from a convulsion. It was observed in those examined immediately preceding and following a convulsion that the waves were more marked at this time.

Of the 24 cases showing waves, 13 were present in cases showing a definite aura, 4 in those showing no aura and 7 in whom a history could

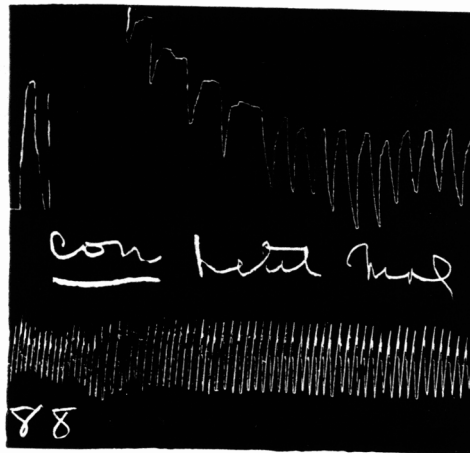


Fig. 2.—Relatively low blood-pressure during petit mal attack

not be obtained. Four other cases showing an aura had no waves. The tracings on these cases were not taken on the day of a convulsion and none of them had a pneumogastric aura.

The duration of the waves ranged from $13\frac{1}{3}$ to 35 seconds. The greater number ranged from $13\frac{1}{3}$ to 26 seconds. The duration of the waves remained constant in each individual, and the series may be divided into three groups possessing waves 13.33 to 18.66, 20 to 22 and 24 to 28 seconds.

Of 39 cases the pulse-rate was slower during the high blood-pressure, in 17 cases, more rapid in 3, and unchanged in 18. It is safe to say that when the pulse changes in rate, it is usually slower during the period of high blood-pressure.

4. Pulse and blood-pressure in relation to the convulsion: It would be useless to give a review of the literature on these points for the reasons

outlined above. Most authors agree that there is an increase of blood-pressure preceding and during the convulsion, that it rapidly falls after the convulsion, but remains higher than normal throughout. The pulse-rate is said by most observers to be increased during the convulsion. Some state that it is slow; it is possible that these cases may be the bradycardias of heart block. Morgenthaler goes further and states that the blood-pressure is labile after the convulsion.

We have obtained tracings showing continuous pulse- and blood-pressure curves before, during and after the convulsions, on three dif-

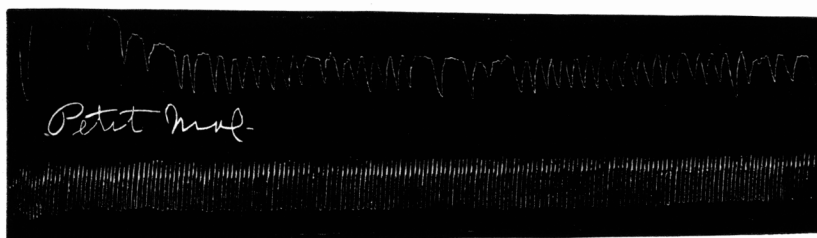


Fig. 3.—Alternating type of respiration following a petit mal attack.

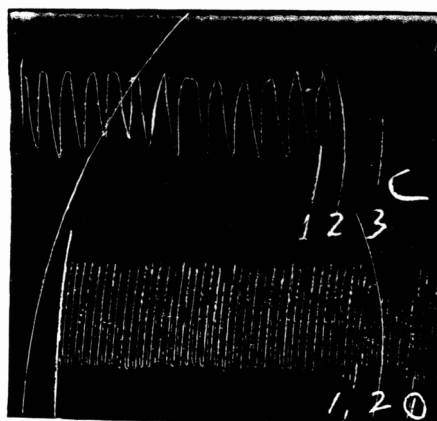


Fig. 4.—Petit mal attack. 1. Drop in blood-pressure. 2. Apnea. 3. Convulsion.

ferent patients, and on one during and after the convulsion. In one case we have obtained eight tracings, showing seven petit mal and one grand mal attack each. In another case two grand mal attacks and in two cases one grand mal attack each. In all of these cases there was seen in addition to the Traube-Hering waves, (1) a preliminary rise in blood-pressure occurring from twenty-six to sixty seconds before the convulsion. Where the rise occurred over thirty seconds before a convulsion the blood-pressure usually fell again slightly; (2) immediately preceding the con-

vulsion by from nine to twelve seconds and in one case twenty-eight seconds (this was a case of grand mal attack) there was a sudden marked drop in blood-pressure lasting from eight to thirteen seconds (Fig. 2). The pulse in every instance became rapid and remained so during the convulsion and for a short time following it. The increase in rapidity of the pulse occurred at the time of drop in blood-pressure. The blood-pressure remained relatively low during the time occupied by the petit mal attacks in all fits, and rose within five seconds after the attack. The blood-pressure rose rapidly and markedly, in many instances showing rhythmical variations, and then gradually subsided to the normal level.

In the grand mal attacks we are unable to state positively whether the relatively low blood-pressure persists throughout the entire attack, because of the interference by arm movements and the consequent late appearance of a regular blood-pressure curve. In one of these tracings it can plainly be seen that the blood-pressure is low for a considerable time during the convulsion. It must be said, however, that in tracings taken during the grand mal attacks the blood-pressure is high at cessation of the attack. In one attack of petit mal type in which we were able to note the beginning of the aura, it was found to follow the drop in blood-pressure by two and two-thirds seconds and to precede the apnea by two seconds.

RESPIRATION

The respiration will be studied from two standpoints: 1. Rhythmical change in type of respiration. 2. The respiration in relation to the convulsion.

In twelve of the forty-four cases of rhythmical change from rapid, regular and shallow, to slow, irregular and deep was noted within a short period preceding and following a convulsion. Eleven of these cases showed well-marked Traube-Hering waves of blood-pressure. The changes in respiration did not have any definite relation to the changes in blood-pressure indicated by the Traube-Hering waves, nor to the blood-pressure in general. A change similar to this has been noted in meningitis by Conner⁷ (Fig. 3).

In five cases one or more periods of apnea were observed lasting from sixteen to thirty seconds. During this period there was seen a fall in blood-pressure and in one case two rhythmical waves of change in blood-pressure. This apnea occurred at times having no bearing on the convulsion.

A study of the respiratory change in relation to the convulsion was possible in five tracings taken during petit mal and three tracings during grand mal fits in three different patients. In every example of petit mal attacks in one patient it was seen that there was a cessation of respiration preceding the convulsion by four to twenty-six seconds, more often four

to nine seconds. The apnea persisted throughout the convulsion and lasted from thirteen to sixty seconds. It was interrupted in a few instances by several deep and irregular respirations. The apnea commenced at the height of inspiration. It was in every instance preceded by the fall in blood-pressure by from two and two-thirds to six and two-thirds seconds.

In the tracings of the three grand mal attacks, in each instance the fall in blood-pressure preceded the apnea, and the apnea preceded the convulsion as in the case with petit mal attacks. We are unable to state definitely how long the period of apnea lasted relative to the convulsion in these cases. The tracings show either an apnea or an apnea interrupted by slow and irregular respiratory movements.

Before taking up the discussion of the relation of our findings to the various theories of the pathogenesis of epilepsy, we shall make a résumé of those conditions which may have a bearing on a causal relation to epilepsy.

There were present a number of diastolic arrhythmias considered to be of vagal origin. A large number of cases showed Traube-Hering waves, especially those cases having an aura. These waves were particularly prominent during the time near or following a convulsion, and practically disappeared after five days.

Rhythmical respiratory movements were found in a considerable number of cases, with one exception always associated with, but having no relation to, the Traube-Hering waves.

The convulsions showed a sequence of events as follows: A preliminary rise in blood-pressure followed by a sudden fall, then an aura, then a period of apnea and then the convulsion. The blood-pressure remains relatively low throughout the petit mal and also probably throughout the grand mal attacks. The pulse becomes rapid with the fall in blood-pressure and remains so during the convulsion (Fig. 4).

The literature on the pathogenesis of epilepsy is especially rich. The theories are numerous and contradictory and the evidence is inconclusive. We shall content ourselves with mentioning some of the theories, first, as to the stimulus that determines the discharge, and second, as to the seat of discharge.

Relative to the nature of the stimulus we shall confine ourselves to the question of anemia and hyperemia of the brain. Anemia of the brain as the cause of unconsciousness and convulsion has been supported by Kussmaul and Tenner, Nothnagel, Riegel and Jolly, Gutnikow and many others. The gap between the several steps of reasoning employed by these authors is considerable.

The facts that anemia of the brain can produce convulsions and that

7. Conner, Lewis A.: THE ARCHIVES INT. MED., 1912, ix, 203.

a pallor of the face has been observed by these authors during the attack, is certainly insufficient evidence to establish anemia as the cause of unconsciousness or convulsions.

On the other hand, hyperemia of the brain has likewise been supported by many, Landois, etc. Recently it has been found that, during experimentally produced epilepsy, hyperemia and not anemia of the brain is present during the convulsion. (Rabinowitch, Berger.) We shall refer to these observations again.

As to the seat of discharge, we have a great number of observers arrayed against one another, one group assuming the medulla and pons to be the site of discharge, Nothnagel, Van d'Kolk, Reynolds, Echeverria, Kussmaul, etc., the other placing it in the cerebral cortex — Charcot, Ferrier, Luciani, Gowers, etc. — while Hughlings Jackson suggests that fits might result from discharge of lesions in either of these two.

It is not necessary to enter into a detailed account of the experimental work tending to prove either of these theories. Suffice it to say that convulsions may be caused experimentally through irritation of either of these regions.

The experimental production of convulsions by irritation of the cortex and the occurrence of convulsions as the result of disease of the cortex has led to the conclusion, as yet unproven, that the greatest number of convulsions originate in the cortex. This does not exclude the medulla and pons as the site of discharge in some convulsions.

J. Hughlings Jackson and H. Douglas Singer⁸ suggest that in addition to the cortical type of epileptic fits, there occur, in the human subject, bulbo-pontine (lowest level) fits, analogous to those experimentally produced in some lower animals. They offer in support of this hypothesis a case showing fits which definitely began by convulsions of the respiratory muscles. Of special interest is the observation that with the beginning of the earliest motion of the convulsion, respiration ceased and was not resumed until the end of the fit, which lasted from forty to sixty seconds.

Harvey Cushing⁹ has contributed some very important data as to the relation between increased intracranial tension, cerebral anemia and respiration. He has found that at a stage during the height of compression there occur Traube-Hering waves, and Cheyne-Stokes respiration associated with rhythmical change in blood-pressure, the low blood-pressure corresponding to the period of apnea. It would seem that the period of apnea is the result of cerebral anemia produced by the increased intracranial tension and the relatively lower general blood-pressure.

8. Jackson, J. Hughlings, and Singer, H. Douglas: *Brain*, 1902, xxv, 122.

9. Cushing, Harvey: *Am. Jour. Med. Sc.*, 1902, cxxiv, 375; 1903, cxxv, 1017; *Bull. Johns Hopkins Hosp.*, 1901, xii, 290.

It can readily be seen that all experiments on the cerebral circulation must take into consideration intracranial tension, and such experiments as include the opening of the cranial cavity without subsequently closing it, must be discarded.

The fact that increased cerebrospinal pressure has been observed during the convulsion of epilepsy (Bianchi,¹⁰ D'Ormea), adds considerable speculative interest to our observations that there is present an undulatory respiration and Traube-Hering waves together with a fall in general blood-pressure preceding the convulsion in all our cases.

It would be important to determine by further work any possible relation between the changes found by us and any change in the cerebrospinal pressure, perhaps similar to the changes found by Cushing in experimentally producing increased cerebrospinal pressure. From our experiments no definite conclusions can be made as to the state of the cerebral circulation at the time of convulsion, inasmuch as the intracranial tension was not measured. A vasoconstriction of the peripheral vessels does not necessarily indicate a similar condition of the cerebral vessels.

Our one case in which petit mal attacks were studied is very similar to the case described by J. Hughlings Jackson and H. Douglas Singer and shows definitely that, whatever the nature of the stimulus, the site of discharge either acts on both the cerebrum and medulla and pons, or on the medulla and pons alone.

The presence of unrest of the vasoconstrictor and respiratory centers shown by the Traube-Hering waves and undulatory respiration, the fall in blood-pressure preceding the convulsion, and the cessation of respiration probably due to vagal interference, as well as the aura of pneumogastric type following shortly after the fall in blood-pressure, all point to the bulbopontine region as a site of disturbance.

The irritation may have commenced at the cortex and spread downward, being felt in the medulla first, or it may have commenced in the medulla and spread upward; in this particular type of case we are of the opinion that the site of discharge is in the medulla. We are unable to say if the same is true of grand mal attacks and obviously cannot make any assertions for epileptic convulsions in general. It is noteworthy that the sequence of events in the petit mal attacks of one patient was the same as that observed in a grand mal attack in the same patient and that two other grand mal attacks in two other individuals presenting a clinical picture of ordinary epileptic convulsions likewise showed similar manifestations.

10. Bianchi: *Ann. di. Neurol.*, 1911, xxix, Part 3.

CONCLUSIONS

It may be stated that with regard to the cases observed by us:

1. There are present in many cases of epilepsy rhythmical variations of blood-pressure other than those due to respiratory movements.
2. The sequence of events relative to a convulsion is as follows: A preliminary rise in blood-pressure followed in series by a sudden drop of blood-pressure, a period of apnea, and then the convulsion.
3. The blood-pressure was relatively low during convulsions of petit mal type and during some of the corresponding period of the fits of the grand mal type.
4. The pulse was rapid during the convulsions.
5. A study of the changes in the respiratory and circulatory systems in some of the cases of epilepsy suggests that the site of discharge is in the medulla and pons (the "lowest level of fits" of Hughlings Jackson). Likewise it points to the medulla as participating in the discharge in all cases of epilepsy whether this discharge originates there or not.

We wish here to express our gratitude to Dr. H. Douglas Singer, director of the Institute, for his encouragement and kind assistance.