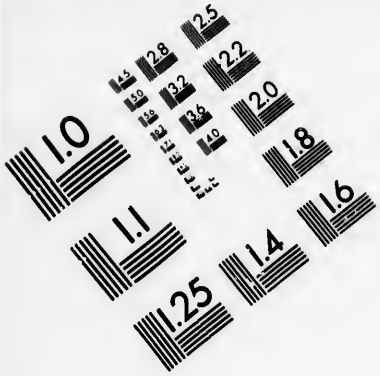

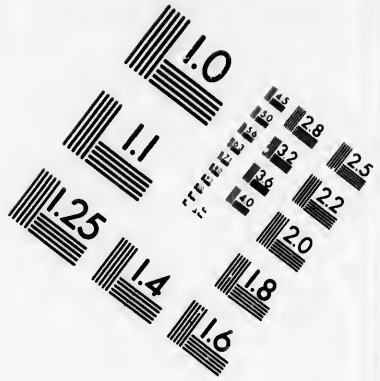

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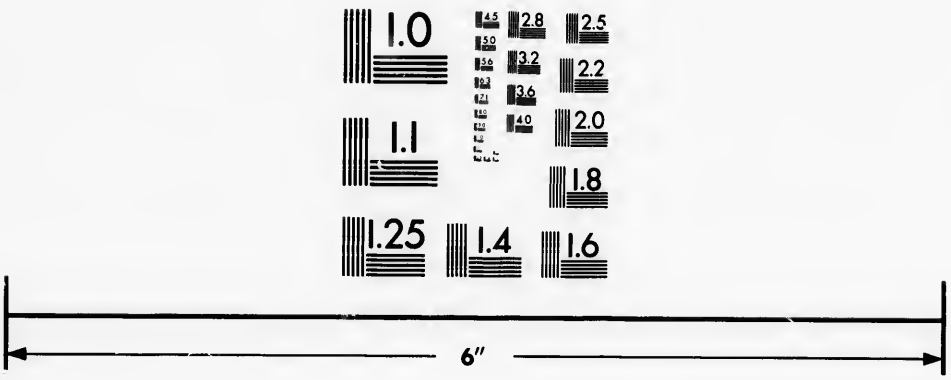

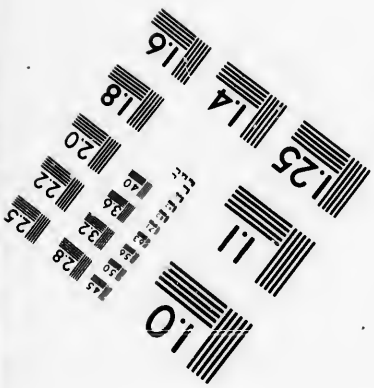

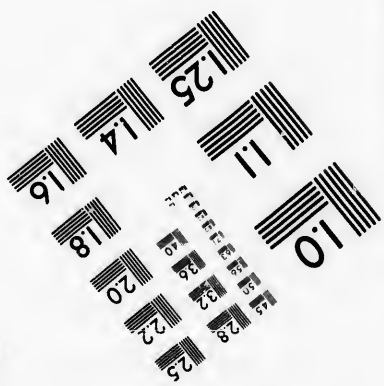

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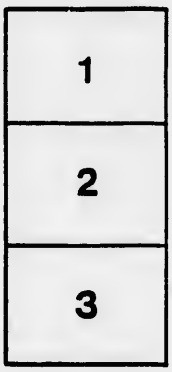

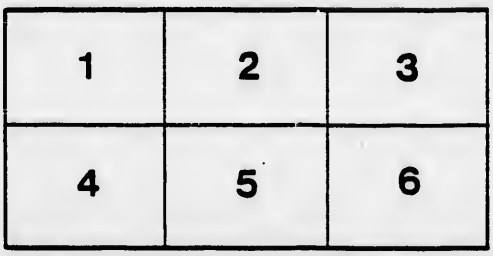

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June 5th, 1897.

A RESPIRATORY SYMPTOM OF TOBACCO POISONING AND ITS EXPERIMENTAL INVESTIGATION.*

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Lecturer on Physiology, McGill University.

THE present paper is written with the object of describing and, as far as possible, explaining a certain peculiarity of breathing met with in cases of tobacco poisoning.

In the experience of the writer it is a very common symptom of excessive use of the "weed," as he has seen three cases in as many years exhibiting it to a marked degree, besides several others in which it was less characteristic. As considerable difficulty was experienced in finding a description of the symptom, it would seem to have been overlooked by most observers, and yet it is believed to be of considerable diagnostic importance. The following are short accounts of the three cases referred to above in which it was most typical:

CASE I.—In December, 1893, a medical student came complaining of palpitation on slight exertion. He said he had used tobacco freely since 11 years of age. While examining his chest his breathing was observed to be peculiar. He would take a deep inspiration, and then there would be little or no breathing for a considerable interval, followed by another deep inspiration. On inquiry he said he believed he often went a long time without breathing. At any rate, he was often conscious of taking a very deep inspiration. He was advised to give up tobacco altogether. He did not do so immediately, and was lost sight of for a time. When seen a year or more later he had given up the habit, and the peculiarity of breathing had passed away. It was this case which first drew my attention to the subject.

CASE II.—L. T., a boy of 14, small for his age, was first seen in December, 1895. He complainced of pain in the left side, extending from the heart around to the back and down the left arm. It was sometimes severe enough to wake him up at night. His mother said he was restless and excitable, and ate poorly. He had smoked cigarettes for two years. While in the office peculiar heaving sighlike inspirations were observed. On being questioned he said he often breathed like that. Discontinuance of tobacco was enforced, it is believed, with success. He was seen at intervals after this, and the breathing did not become normal for over six months, during which the sighlike inspirations were frequently observed. The following case was only diagnosed by the light thrown on it by the two preceding.

CASE III.—In December, 1896, Mr. T., a medical student, came complaining of not being able to take a deep breath. The difficulty had come on three days before, and was increasing. He said he was not prevented by pain, but it felt as if the air would not go in. When asked to try, he seemed to succeed very well, and as he sat in the office he took at intervals deep heaving breaths. He was conscious of effort in doing so. Once he remarked that the air seemed to go in that time. There was no pal-

* Read before the Montreal Medico-Chirurgical Society.

pitation or pain in the chest or arm. The pulse was 70. He said at first that he did not smoke much, but afterwards admitted that he had smoked far more than usual during the preceding week. One afternoon he had smoked seven cigars, and he was not used to smoking more than one or two. He said also that he chewed the ends of his cigars. He was told to stop tobacco and to report progress, but he did not return. A brother practitioner has, however, seen him since, and tells me that the peculiar breathing only lasted a few days after the smoking was discontinued.

The only satisfactory description of this symptom that I have been able to find is in a paper by Chapman, of Louisville, read at the Mississippi Valley Medical Society in 1891 (abstract published in the *Medical Record* and in *Sajous Annual*.) He described the breathing in a case of tobacco poisoning as irregular, consisting of several short shallow respirations, followed by one deep and gasping. He counted the respirations, and found them 20 to 22 per minute. I have to plead guilty myself to having failed to observe the kind of respiration intervening between the special deep inspirations to which I am drawing attention. As far as could be judged from the abstracts at my disposal, Chapman made no attempt to explain the peculiar breathing he described, and after a fairly careful search no explanation was found in the English literature within reach. Such a change in the breathing is in all probability due to some influence affecting either the respiratory centre, the pneumogastric nerve, or the blood.

It has been affirmed by many writers, though denied by some, that changes do take place in the blood in nicotine poisoning. It would seem, however, that any such explanation of the symptom in question may be excluded when we remember that in one of my cases the symptoms persisted for some months after cessation of the use of the drug.

In order to determine whether the respiratory centre or the pneumogastric nerve is chiefly affected, a somewhat detailed knowledge of the effect of tobacco on respiration is required, and as I could not find answers anywhere to some of the questions suggested by these cases, I decided to carry out a few experiments in the hope of settling the matter for myself.

Before describing the experiments I will take the liberty of reminding you in a few words of the principal factors in the nervous control of the respiration. There is a respiratory centre in the medulla which is divided physiologically into an inspiratory and an expiratory centre so distinct from one another that either one may be affected by stimuli which fail to influence the other. These centres may or may not be able to act automatically, bnt they are in any case profoundly affected by nervous impulses reaching them from the brain above and by various paths from below, especially by the pneumogastric nerves. The respiratory centres send their stimuli to the muscles of respiration by the ordinary spinal nerves such as the phrenics and intercostals. The experiments were carried out to determine as far as possible which parts of the nervous mechanism of respiration are affected in tobacco poisoning.

The apparatus used consisted of the well-known arrangement of Marey's tambour, shown in Fig. 71 of the sixth edition of Foster's *Physiology*. By this the movements of the air in and out of the chest can be recorded on a moving surface. A lever scratches curves on a strip of lamp-blacked paper in such a way that the upstroke of the curve reading from left to right corresponds to expiration, and the down stroke to inspiration. The amplitude of the curves is propor-

tionate to the force of the respirations. The records may be preserved by varnishing the papers on which they are taken.

The first point investigated was the effect of tobacco on the respiratory curves of rabbits. For this two experiments were performed, in each of which the rabbit was first etherised. Tracheotomy was then performed and connection made with the apparatus. The rabbit was then poisoned by one or more doses of an infusion of tobacco, and then records were taken of the breathing at intervals. In one case the tobacco was given in repeated doses hypodermically, and in the other one large dose was given by enema.

FIG I.

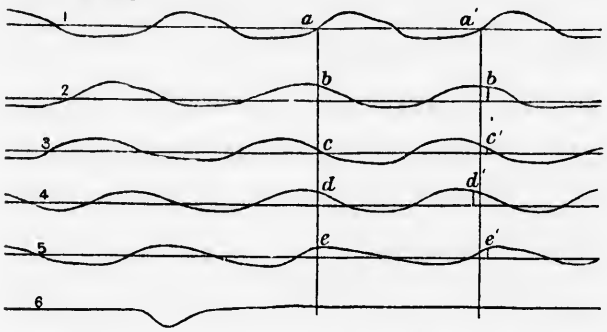

Fig. 1. Respiratory curves from a rabbit poisoned with tobacco: 1. Control—rabbit under ether. After this curve was taken, tobacco infusion was injected into the bowel, and enough ether given at intervals to keep the animal quiet. 2. Lengthening of curves showing slowing of respirations. Taken three minutes after injection. 3. Taken two minutes after 2; and 4, taken three minutes after 3, show the breathing becoming quicker again. 5. Taken five minutes after 4, shows slowing and change of type. 6. Taken five minutes after 5, shows failure of expiration. Respiration reduced to inspiratory gasp. See also Fig. 4, tracing 4.
General description of figures.—Read from left to right. Up stroke corresponds to expiration. Down stroke to inspiration. Base line marks position of lever at rest. In tracing 4, Fig. 3, the base line is a fraction of an inch too high. The vertical lines in some of the figures are through corresponding parts of the curves for comparing the rate of respiration.

The effects which followed are shown in Fig. 1, and were: (1) Slowing of respiration; (2) quickening to beyond the original rate; (3) slowing again and shallowing; (4) a change in type in which expiration became absolutely passive, and the breathing consisted of an infrequent deep inspiration, gasping in character.

The next experiment was carried out to determine whether any of the above effects were due to differing degrees of ether anæsthesia. The results are seen in Fig. 2, and show that the preliminary slowing was probably due to the ether partially passing off, but the ether failed to cause the great quickening seen in the tobacco experiments or the still more characteristic breathing of the later stages.

The third point investigated was the effect of poisoning with tobacco after first cutting the pneumogastric nerves (see

Fig. 3). The results were (1) quickening and increased amplitude; (2) slowing and weakening; (3) failure of expiration, and confinement of breathing to active inspiration and purely passive expiration. This is practically the same series of changes as with the pneumogastrics intact, showing that the characteristics effect of tobacco poisoning are not likely to be due to any effect on the peripheral pneumogastrics.

FIG II.

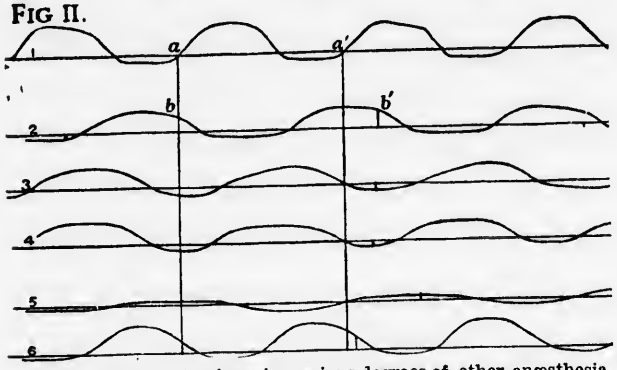

Fig. 2. Respiratory tracings in various degrees of ether anæsthesia. 1. Rabbit well under ether. 2 and 3. Partly out, showing resemblance to the first slowing in the curves of tobacco poisoning. 4. Partly under again. 5. Very deeply under. 6. Partly out again.

Next a rabbit was poisoned as before with tobacco, and the intact pneumogastrics were stimulated at intervals with a faradic current (see Fig. 4). The effect of the stimulation

FIG III.

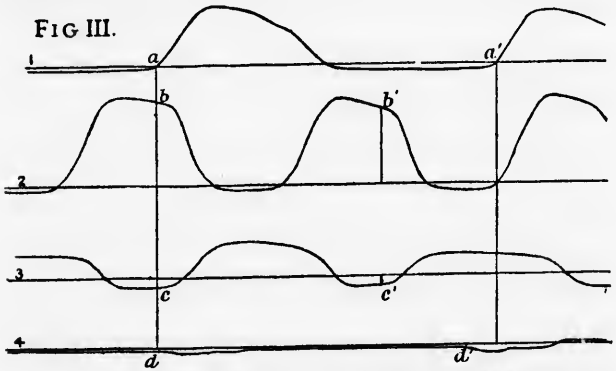

Fig. 3.—Tobacco poisoning after section of both pneumogastric nerves. 1. Respiratory tracings taken after section of these nerves. 2. After an injection of tobacco infusion showing preliminary stimulation of respiratory centre. 3 and 4. Slowing and weakening, with failure of expiration before inspiration.

was at first to stop respiration, or in some cases to render it very shallow and rapid, but towards the end the effect became less marked, and in the final stage of poisoning stimulation

of the nerve failed to affect respiration to any appreciable degree although inspirations were still taking place.

This showed that there was loss of irritability either in the nerve itself, or in the nerve roots, or on the sensory side of the respiratory centre. It is hard to decide for certain which,

FIG IV.

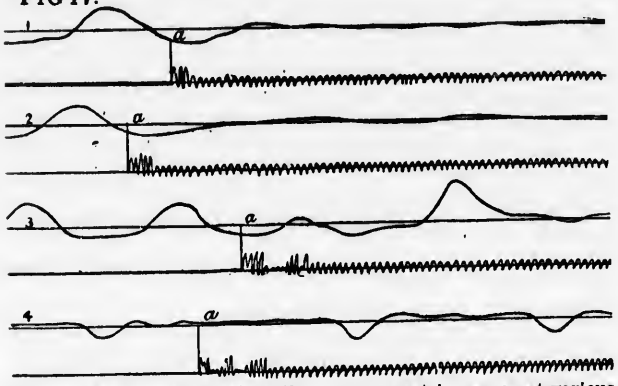

Fig. 4.—Effect of stimulating the pneumogastric nerves at various stages of tobacco poisoning. In each curve (a) marks the point at which a moderately strong current from a Du Bois-Reymond inductorium was turned into the nerve. At first the breathing is stopped or greatly modified, but in the final stage of poisoning seen in Tracing 4 the stimulation has no effect.

but I believe that the profound change in the breathing at this stage may be attributed with reason to all the afferent impulses being cut off from the centre, so that it was only stimulated to action in an imperfect way by the impure blood which reached it. This assumption is borne out by the work of Loewy, as referred to in Landois and Stirling's *Physiology*.

FIG V.

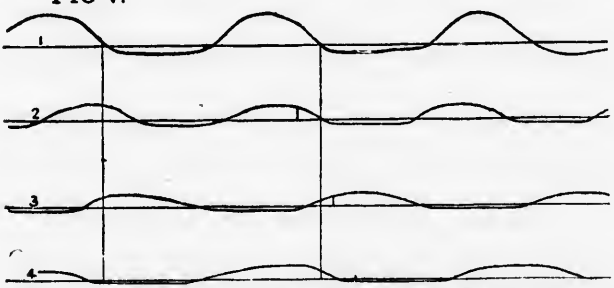

Fig. 5.—Stages of chloral poisoning, shows weakening and slowing o respiration following a preliminary quickening. The failure of inspiration is, if anything, more marked than that of expiration.

He found that on cutting off all possible nervous impulses from the centre the respiration became extraordinarily slow, and each individual respiration became deeper. He believes that these respiratory movements were due to the stimulation

of the centre by the blood. He says that in these cases the total volume of air respired was diminished, as it evidently is in the later stages of tobacco poisoning, and this has been shown not to be the case where the pneumogastric stimulation of the centre alone is cut off.

To return to our experiments. A rabbit was next poisoned with chloral, and the tracings taken which are shown in Fig. 5. These show that in respiratory failure expiration does not necessarily fail first, as in chloral poisoning the reverse seems to be the case. After this an experiment was performed which showed that the trunk of the pneumogastric is able to conduct nervous impulses after death from tobacco. A frog's nerve connected with a muscle was laid upon the upper end of the pneumogastric, and the lower end stimulated with a moderate current. The frog's muscle contracted, showing that a nerve impulse had travelled up the trunk of the pneumogastric, and the electrical changes which accompany every nervous impulse had stimulated the nerve going to the frog's muscle. When the pneumogastric was bruised midway the experiment failed, showing that the result had not been due to escape of current.

FIG VI.

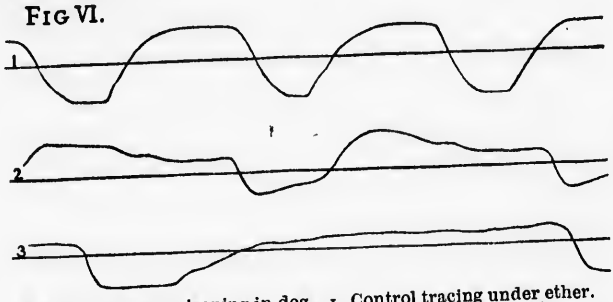

Fig. 6. Tobacco poisoning in dog. 1. Control tracing under ether. 2 and 3. Successive stages of poisoning with tobacco infusion.

Paralysis of the phrenic nerve was next excluded by the fact that after death from tobacco stimulation of the nerve caused contraction of the diaphragm. Control experiments were done on dogs, all hitherto mentioned having been performed on rabbits. Tobacco was administered to two dogs, and tracings taken, of which one series is shown in Fig. 6. Although these are described last they were really among the first performed, and in my inexperience I waited too long before taking my second tracing. This probably explains the fact that the stage of quickening is not shown; but the final and most characteristic stages of slowing and expiratory failure, with deep, gasping inspirations, are well seen. For purposes of comparison and control other experiments were performed on rabbits, determining the effects of varying degrees of asphyxia and opium poisoning, and also of cutting and stimulating the pneumogastrics, etc., but as they have no special bearing on the central theme of this paper they are only mentioned.

From these experiments we reach the following conclusions:

In experimental poisoning, as in the clinical cases reported, the inspiratory phase of respiration becomes more pronounced and expiration less.

Tobacco does not produce this characteristic effect through the peripheral endings of the pneumogastric nerves, as its action is practically the same after those nerves have been cut. The same experiment makes it unlikely that it acts through the trunks of these nerves.

Moreover, they seem capable of conducting nerve impulses after death from tobacco, and it would be difficult to explain the diminution which seems to occur in the total volume of air breathed by any action on these nerves.

I do not deny that the pulmonary branches of the pneumogastrics may be affected in any way. On the contrary, Roy and Graham Brown have shown that nicotine dilates the bronchial tubes, presumably through these nerves, but the characteristic symptom forming the subject of this paper cannot be explained by any action of the poison on them.

The poison seems to act principally on the respiratory centre, paralysing the expiratory division of it, and rendering the whole centre insensitive to afferent nervous impulses. The deep-drawn inspirations seen in my three cases may correspond exactly to the deep-drawn inspirations seen in the rabbit and dog in the final stage of poisoning, but from the fact that respiration may be carried on in a feeble way between them, and that they are seen in cases of moderate degrees of poisoning, it seems more likely that they are due to a less severe interference with the sensory side of the centre causing a partial failure of response to the ordinary stimulating influences from above and below. This properly brings into play direct stimulation of the centre by the blood from partial asphyxia, which explains the subjective feeling of lack of air complained of in Case III.

Summary and Application.

A fairly common symptom of tobacco poisoning is a deep gasping inspiration occurring at intervals, and sometimes quite audible. This may be practically the only symptom complained of. It is probably due to a paralysing action of the drug on the respiratory centre, affecting especially the expiratory division, but also diminishing the irritability of the whole centre to afferent impulses. This symptom may persist from a few days to some months after the poison is discontinued.