Pyridine in the Treatment of Asthma.

BY

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PYRIDINE

IN THE TREATMENT OF ASTHMA.*

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It was at the instigation of my colleague, Dr. J. C. Wilson, that Mr. Louis Genois, Pharmacist, 1410 Walnut Street, first procured this drug, and to him I am indebted for its use. Pyridine has been known in chemistry for some time, Etarde and Cahours having discovered a pyridic nucleus in nicotine in 1880. Its use in medicine, however, is novel, as the first mention of it was made in a paper read by Germain Sée before the Academy of Sciences last June. He had remarked so frequently the benefit derived from empiric and secret formulæ, to which he was so often forced to resort, that he endeavored to ascertain the true physiological agent to which these results could be traced. Together with Bochefontaine, he instituted a chemical analysis, showing that their action was due to a uniform base developed by the combustion of certain plants and alkaloids, as, for example, chinonine, pilocarpine, atropine, nicotine, and morphine. It has also been found by Wohl and Eulenberg ("Bulletin gén. de thérapeutique médicale, chirurgicale,

* Read before the Philadelphia County Medical Society, January 27, 1886.

et obstétricale," June 30, 1885) in the condensed products of tobacco-smoke, and during the destructive distillation of dry organic matter in the products of bony tissue and coal tar.

The name pyridine is derived from the Greek word πῦρ (pyr), meaning fire, indicative of its source of preparation; when pure, it is a clear, colorless liquid, with a specific gravity of 96, boiling at 274° F., inflammable, having a strong penetrating odor, evaporating in the air at ordinary temperatures, and miscible with water in all proportions. Its chemical formula is C_5H_5N, being that of a base belonging to a series of bases of which picoline (C_6H_7N) and lutidine (C_7H_9N) are the most important, being analogous to the aniline bases, and it forms salts with the mineral acids, which are very soluble but easily disintegrated; the latter constitutes one of its difficulties in administration. Sée's* experiments show that the sensibility of the pneumogastric nerve and the excitability of the medulla oblongata are decidedly diminished in the dog. "The blood-pressure, which is 14° ctm. of mercury in the normal state, rises to 32° ctm. upon central excitation of the pneumogastric, severed in the neck. After the injection of one gramme of pyridic nitrate, practiced twenty times, the arterial tension gradually fell, and, if centripetal excitation was repeated, the pressure remained unchanged—that is, the gray substance of the spinal cord had lost its reflex power."

Physiological experience at first would indicate a similarity to the action of nicotine—contraction of the pupils, dyspnœa, convulsions, and death; this I have not found as yet to be the case. Owing to my inability to procure a proper combination for internal use, I have been compelled, in administering it to the lower animals, to use it in the form of vapor, and the observations are not sufficient to warrant

* "Bulletin générale de thérapeutique," June, 1885.

positive conclusions; but I would express the opinion that in the healthy animal the respirations are at first quickened, then slowed, the pupils are but little affected, there are no convulsions or dyspnœa at any time, but drowsiness and stupor. The respirations become slower and slower until they cease. After death the heart continues to beat for a considerable period, the cavities containing black fluid blood.

The method of administration is by inhalation, as it can not be given by the mouth or subcutaneously, owing to its excessive irritative action in the first place, and to the instability of its salts in the second. The direct application of the drug to the nose or mouth provokes nervous troubles, as well as irritates the mucous membrane.

I have suggested the use of capsules, but its volatility prevents the closure of those made of glass, and its permanence in those made of gelatin. I think that proper combinations may be made to be inhaled directly from a bottle or towel. I have used from two to four grammes at a sitting, poured upon a saucer, placed in one end of a small room with doors and windows closed, or, what is better still, a large closet, and allowed the patient, sitting a little distance from it, to inhale the pyridic vapors mixed with the air. The absorption is immediate, the drug being detected in the urine in a few moments.

Upon the healthy adult, as shown in myself, assistants, and nurses, there has been almost universally a flushing of the face, with quickening of the pulse and respiration, the latter lasting but a few moments, the former from fifteen minutes to ten hours, depending largely upon the length of time of inhalation. In several instances temporal headache of a slight character has persisted for several hours; at times a peculiar full sensation approaching giddiness is experienced.

The fact that in the healthy the pulse and respiration

are quickened for a few minutes does not hold good in asthmatic patients, for, almost without exception, the heart's action, which previously may have been accelerated, slowly falls to the normal, without change in character or rhythm; and less rapidly the respirations, which become slower, easier, and more full, the intense longing for air disappearing, with diminution of the oppression.

In most cases there is a desire to sleep, which in some becomes irresistible; this resembles, however, normal sleep, from which they are easily aroused, and without insensibility or loss of intelligence, thus distinguishing it from the sleep produced by narcotics and anæsthetics, although there is a slight loss of muscular reflex action.

I have used this preparation many times in a series of twelve cases of asthma. Brief histories of a few will, however, serve to show its clinical action. [For the careful attention to every detail in taking notes on many of the following cases I am indebted to Dr. D. H. Lake and Dr. John Da Costa, resident physicians in the Philadelphia Hospital.]

Case I.—Jane T., aged sixty-five, white, admitted to Philadelphia Hospital (Ward 2, bed 12) early in October, 1885. Has suffered for many weeks from severe asthmatic paroxysms; restless and wakeful at night; spends most of the time sitting up, occasionally rushing to the window for air. Complains also of a constricted feeling around the chest. Kidneys normal; lungs are slightly emphysematous; heart shows advanced muscular degeneration. Patient was placed upon quebracho with slight benefit, but, owing to nausea, she refused to continue its use.

October 15th.—During a paroxysm, respiration 42; pulse very weak, 84; one gramme of pyridine was prepared for inhalation. After five minutes, pulse was 80, respiration 30; fifteen minutes, pulse 78, respiration 24. Breathing became easy and lost its irregular character; cheeks red; in twenty-five minutes seemed half asleep; respiration 20, pulse 78, strong. She was put to bed at once; fell asleep. Four hours after, was still sleeping, but it

was not profound, as she awoke on the doctor feeling her pulse, but went to sleep immediately after. Cheeks still red; slept the remainder of the night.

The following day respiration and pulse normal.

October 20th.—During past five days there has been no return of paroxysms, some little dyspnœa occurring on exertion. Present time quite a severe onset; before inhalation, pulse intermittent, 96; respiration 36. Grm. 3 pyr. used at 3.15; 3.35, pulse 84, regular, and fuller, breathing, twenty-two times per minute, quiet and without exertion. The last sitting took place October 25th, the patient being discharged a few days later entirely free from asthmatic attacks. She still had slight dypsnœa upon exertion. (Fatty heart.)

Case II.—Anne D., aged fifty-two, chronic bronchitis, with morning asthma. Admitted to Philadelphia Hospital (Ward 2). The iodides were not tolerated; quebracho gave but slight relief; morphia, however, was of decided benefit.

October 23d.—Two grammes of pyridine were used at 10.45. Pulse 90, respiration 38, great distress in obtaining air; 10.58, pulse 84, respiration 21; 11.05, pulse 78, respiration 18; 11.15, after cold air had been allowed to enter room for five minutes, owing to the oppressive heat of the apartment, the pulse was 102, respiration 24 (evidently due to excitement).

Breathing was very irregular, cheeks red; complained of feeling dizzy, and, on endeavoring to stand up, fell over. In a few minutes she started to walk, which she did like a person intoxicated. She was drowsy and inclined to sleep all day, but felt very comfortable and much relieved.

25th.—Next paroxysm, pulse 90, respiration 34 and extremely difficult. After fifteen minutes, pulse 84, respiration 24, comfortable, with no repetition of unpleasant symptoms previously experienced. This patient had but one attack up to November 1st, when she insisted upon being discharged, feeling able to resume her duties as domestic.

She was readmitted in December on account of severe cold. I may add that there was some dilatation of the bronchial tubes, with bronchorrhœa. Although under constant observation to the present time, there has been no return of asthmatic seizures.

Case III.—Sallie K., aged forty-four, admitted January 13, 1886 (Ward 2). Asthma dating from childhood, never having been free from attacks for over a month at a time. There were marked emphysema and some dilatation of the tubes; patient was robust and apparently well nourished. Being thoroughly conversant with the therapeutics of this disease, she stated that she never had relief from any drugs—commenting upon a large number—except the iodides, which she had been taking off and on for twenty-seven years.

January 22d.—A severe paroxysm occurred. Respiration 44; pulse weak, 120; body bathed in a cold sweat; some cyanosis. After using 2 grm. of pyridine for twenty minutes, the breathing became normal. After inhalation the patient walked up three flights of stairs without trouble. No drowsiness.

24th.—Was seized while in the hospital yard with another severe attack. She was again in great distress, and occupied fifteen minutes in walking 150 yards to the room for inhalation, where 2·8 grm. of pyridine were used. Upon entering, pulse 144, respiration 32, very labored, great depression, and cyanosis. After thirty-five minutes, respiration 24, pulse 108; wheezing absent, and breathing free.

Case IV.—Annie ——, colored, admitted January 23d to the Philadelphia Hospital, with advanced syphilitic phthisis. Very much exhausted, pulse 120, weak, and compressible. History of daily asthmatic seizures for some time. Breathing labored, not increased in frequency. She was allowed to inhale the vapor from 2 grm. of pyridine for five minutes, at which time there was no change in the character of the respirations, and, as the pulse was still weak and very compressible at 100 per minute, the patient was removed to the ward.

Case V.—W. A., male, aged twenty-eight (private practice). Nervous pulmonary asthma, poorly nourished, anæmic, subject to frequent attacks of bronchitis; no emphysema or organic disease. Family record phthisical. Had marked paroxysms for one week, recurring in the mornings between two and four o'clock. The remedies in general use were employed, for comparison, during five mornings, including fluid extract of quebracho, lobelia, the various fumes from burning pastils, stra-

monium, etc. Notwithstanding treatment, the patient was never able to sleep after the onset, with the exception of the fifth day of treatment (or thirteenth of the disease), when morphia was administered hypodermically. The following night he inhaled the vapor from 3 grm. of pyridine placed in a large closet. At first, owing to fright, the pulse, and with it the respirations, were slightly quickened, but after five minutes both became slower. In fifteen minutes respirations were perfectly free. He was allowed to remain fifteen minutes longer, when he returned to bed complaining of some temporal headache and drowsiness. He slept until his usual time of rising, when there were no unpleasant symptoms. The next night the paroxysm returned a little later than usual. The drug was administered as before, with the same beneficial effect. This time there was no acceleration of pulse or respiration upon starting the inhalation, nor was any headache noted, although drowsiness was present after a sitting of twenty-five minutes.

The following night no well-marked seizure occurred, although the patient took a séance of fifteen minutes.

A mild attack occurred the next night. Inhalation as before.

Three nights following, did not awaken.

Thirteenth night of treatment he awoke at 4 A. M. and stated that he felt oppressed, when he resorted to the remedy as usual. There was no typical seizure, and I am inclined to think there was no threatening of any. There has been no return of asthma since, the last paroxysm occurring December 19th.

These few cases will serve as an illustration of the twelve that fell under my observation. Four were in females, eight in males; the ages ranged from twenty-six to sixty-five, divided as follows:

Nervous pulmonary asthma, 3. No return of attacks in any.

Cardiac asthma, 3. All were relieved of attacks. One remained under observation three months, and one for two weeks only.

Bronchial asthma, 3. In one there was no return during ten weeks' stay in the hospital. The two others were relieved of their attacks and insisted upon their discharge, being under treatment less than three weeks.

Asthma in advanced phthisis, 2. In one there was but slight relief during the paroxysm; in the other there was absolutely no benefit.

Asthma as a complication of gout, 1. No return in a month. Albuminuria from interstitial nephritis was present.

Of the fourteen cases reported by Sée, four were in females, ten in males, from thirty to sixty-eight years of age. Nine were what he terms "pure asthma," all of which were more or less relieved, and five cases of cardiac asthma.

In one case of twelve years' duration pyridine caused nausea and vertigo after eight days of treatment, which necessitated its discontinuance, although great relief was obtained. Nausea I have not seen; vertigo but once.

In one or two cases where the expectoration had been purulent it lost that character after the inhalation.

All unpleasant symptoms seem to be confined to cases with long-standing emphysema, or valvular or degenerative heart disease, with small, irregular pulse. In young, robust people with "simple" pulmonary asthma there seems to be drowsiness alone.

Since these observations * were made I have noted, in a more recent report by Lublinski,† one case of marked tremor of the limbs with nausea, and another with vomiting, dizziness, and severe headache. In all of these, however, the length of time of each inhalation was prolonged from one to one and a half hour.

* Report of a clinical lecture delivered November 11th at the Philadelphia Hospital. "Medical and Surgical Reporter," December 5, 1885.

† "Deutsche Medizinal-Zeitung," Berlin, November 5, 1885.

The beneficial results obtained from this remedy seem to be from its action on the sympathetic and the medulla.

Any depressing effects on the heart noted in Case IV would seem due rather to the interference with the pulmonary functions, death being caused, in the lower animals at least, by paralysis of the respiratory centers.

Pyridine is not to be classed as a curative agent. Most likely its greatest value will be seen in cases of simple or nervous pulmonary asthma, when the iodine preparations can not be borne, or nitro-glycerin and sodium nitrite are contra-indicated. Although in the bronchial or catarrhal forms of the disease the relief of the paroxysms has been marked in ninety per cent. of the cases treated, of the remaining number nearly all had emphysema of long standing.

In asthma occurring in advanced phthisis the drug should be given with care on account of the small amount of lung tissue left unaffected, especially where there is a great degree of consolidation with fibroid induration, as in Case IV, when, perchance, the spasm may be relieved, but few air vesicles remain in condition to respond. Here at least morphine will hardly be superseded.

I have used pyridine in several forms of dyspnœa occurring in different diseases without much benefit.

In phthisis the recurring dyspnœa and orthopnœa are relieved during the period of inhalation only, returning in a few moments, and at times with increased violence.

With so little experience, this drug must be administered with a certain degree of caution until its action is thoroughly understood, severe or persistent headache, nausea, vomiting, and vertigo acting as danger signals, warning us to proceed with care.

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