TOBACCO SMOKE.

ITS CHEMICAL COMPOSITION AND PHYSIOLOGICAL EFFECTS.

H. PLITTLE. A THESIS

B. S. SCHOOL OF CHEMISTRY.
Tobacco smoke is poisonous.
In the smoke from the mildest varieties of smoking tobacco there appears to be but little nicotine as compared with native tobacco, but this does not bear in any way upon the fact that there are other poisons in the smoke, which, although they do not act as rapidly as nicotine, are still nonethe less injurious. In fact a large number of true poisons have been separated, and their composition determined by persons of very high reputation as chemists, among them LeBou and Noel, Voelk, Liebling and Hülse. According to Richardson tobacco smoke contains Pyridine, $C_5H_5N$, the lightest, and Viridine, $C_2H_9N$ the heaviest of the volatile alkaloids, and between these Picolide, $C_6H_7N$, Lutidine, $C_7H_9N$, Collidine, $C_8H_11N$; Parvoline, $C_9H_3N$; Corodine, $C_{10}H_{15}N$; and Rubidine, $C_{11}H_{13}N$, besides ammonia, hydrocyanic acid, 1 Diseases of Common Life, p. 215.
Pyroiligneous oils; a series of oily bases yielding ammonia when acted upon by ethyl iodide; several compounds of carbon, hydrogen and nitrogen analogous to aniline; carbonic acid and carbonic oxide gases; Reine, jume, water, and free carbon. The author adds, however, that not all of these substances will be found in any one specimen of smoke.

An article in Comptes Rendus states that Le Bon and Noel recently presented to the Academy of Sciences at Paris, three flasks, containing poisons extracted from tobacco smoke.

The first flask contained hydrocyanic acid.

The second an alkaloid possessing extremely poisonous properties, 25 of a drop having proved fatal to animals in several cases.

The third flask contained an aromatic principle, the composition of which has not yet been
accurately determined. This substance, together with the alkaloid before mentioned contribute very largely to the perfume of tobacco smoke. The alkaloid, although it has the same chemical composition as Colidine, is much more intensely poisonous. LeBou and Noel express the opinion that these three poisons should not be overlooked in computing the injurious effects of tobacco smoke. Their presence would certainly account for the poisonous effects of smoke from tobacco which contains but little nicotine.

Experiment No. 1.

Five grams of ordinary smoking tobacco were placed in a Bohemian glass combustion tube, and heated to redness, the combustion and distillation products being passed through a solution of sulphuric acid of known strength. The solution was then
completely neutralized by means of a standard solution of potassium hydroxide, a known amount being added. The difference between the amount of acid neutralized by the potassium hydroxide and that contained in the original solution was taken as the amount neutralized by the nicotine and other alkaloid contained in the smoke. This was 30.1583 per cent. of the original weight of the tobacco taken. It was discovered, however, that the heat used was much greater than is ever attained in the ordinary process of smoking. Tobacco in a pipe or cigar, and no air had been admitted during the process; it was concluded that the nicotine, empyromatic oils, etc., which would have been burned up in the process of ordinary smoking, had been simply decomposed, their elements forming strongly alkaline substances.
which had assisted in neutralizing the acid.

Experiment No. 2.

One-fourth of a pound of tobacco was placed in a Heerian crucible having an orifice at the bottom connected with a small glass tube. The tobacco was lighted, and the smoke drawn, by means of a Bunsen's air pump, through a column of pure water one inch square, and sixty inches high. After the tobacco was entirely consumed this solution was treated with a standard solution of potassium hydroxide, as before. The percent. of alkaloid found by this process was 7.7381. Now, however, it was discovered that ammonia was present in the solution in considerable quantities, thus vitiating the results.

Experiment No. 3.

One hundred grams of smoking tobacco were placed in an ordinary clay pipe, a few grains of
At a time and ignited, the smoke being passed through a series of Geisseis bulbs, by means of a Bunsen's pump. The solution was then boiled to expel ammonia, and the amount of potassium hydroxide necessary to completely neutralize it added as before. The per cent. of alkaloid found by this process was 1.0897. It was soon discovered, however, that nicotine, and probably other poisonous principles of the smoke, pass off, with steam, at 100° Centigrade, thus destroying the data obtained by this experiment.

Experiment No. 4

The specimen of tobacco used in this experiment was obtained from J. Buhr, of Gifford, Ill. It was somewhat rank in growth, and extremely strong in quality. One half pound of this tobacco was ignited in common clay pipes, the smoke being passed through a series of twenty
eight test-tubes, each of which contained
twelve and a half cubic centimeters of pure water.
The solution was then removed from the tubes,
and divided into four parts, 100 C.C. for the estima-
tion of nicotine, 100 C.C. for the estimation of empy-
omatic and pyroligneous oils, and pyridin, 100 C.C.
for the determination of carbon, resins, and gums,
and 50 C.C. for general qualitative work, and as a
reserve in case of accident. The 100 C.C. for the estimation
of nicotine was shaken up in a stoppered flask
with 8 g. of pure ether. The etherial solution was
then decanted, and the ether removed by evaporation.
Acetic acid was then added to keep the ammonia
in solution, after which the nicotine present was
precipitated with mercuric chloride. The precipitate
was then collected on a filter paper of known
weight, washed, dried three hours at 100° C., and weighed.
The percent of nicotine thus obtained was 7314.

The great advantage of this process is that the ammonia is not precipitated with the nicotine.

Physiological Effects.

The 100 C.C. reserved for the purpose were shaken up with four ounces of pure ether, the ethereal solution decanted, the excess of ether got rid of by evaporation, and the residue, which consisted of a dark syrupy mass, was placed in a hypodermic syringe and injected into the fleshy portion of the leg of a large terrier dog. Almost instantly the breathing became very laborious and rapid. Severe nausea and vomiting at the end of one minute. Eyes somewhat dilated. Pulse rapid and irregular. Very free perspiration, especially at the nose. At the end of two minutes a spasm occurred, after which life appeared to be extinct. The animal soon began to show signs of
consciousness, however, and at the end of forty
minutes appeared to have completely recovered.
At the end of forty-five minutes after the adminis-
tration of the poison violent symptoms again
appeared, in the following order: 1 A violent spasm
accompanied by violent trembling. 2 A few moments
of unconsciousness. 3 Another violent spasm
lasting 1 minute, and terminating in profound
coma, which continued until death supervened.
Time which elapsed between the administration
of the poison and the death of the animal one hour,
one and a half minutes.

Post Mortem Appearances.
The brain was super-charged with dark blood.
Under the microscope both the white and the gray
matter of the brain appeared to be perfectly normal.
Not the slightest trace of any alkaloid precipitable
by P.T.O.G., was found in the brain.
The lungs were extremely pale and destitute of
blood. The liver was much congested, and of a
very dark color. The inner wall of the stomach
presented a very peculiar appearance, being covered
with bright red spots about three centimeters
in diameter. Kidneys normal externally, but
much inflamed along the inner surfaces of the
blood-vessels. The urine gave a distinct test
for nicotine. The valves of the heart, and the
lining membrane of both auricles and ventricles
much inflamed, as were also the pulmonary
artery and pulmonary vein, and the aorta.
The blood was very dark in color, very fluid, and
gave a distinct test for nicotine.
The portion of the leg into which the poison
was injected was extremely turgid and very
highly inflamed. There was a dark spot about four centimeters in diameter where the poison was injected. All the muscles of the body were tense and rigid, both before and after death. The poison appears to have acted on the nerve centers rather than to have produced any particular structural changes in the tissues of the body. There was no evidence of any portion of the body having been disintegrated by the poison in any case.

Resin.

When the 100 c.c. of smoke solution was shaken up with ether in order to remove the soluble poisons for the determination of physiological effects a dark layer of a pitchy, black substance appeared between the two liquids. In order to determine the composition of this
substance the liquid below it was siphoned off and the residue digested for twelve hours with pure chloroform. The chloroform solution was then removed, and evaporated to dryness. The dried residue was then subjected to an ultimate analysis. Result—Carbon 79.98, Oxygen 10.67, Nitrogen—by difference—9.35 This yields the formula C66H46N.

The mass left in the process of extraction with chloroform was dried at a temperature of 100°C. for four hours, and then placed in a glass combustion tube with pure dry copper oxide, and subjected to an intense heat, the vapor being passed through calcium chloride tubes and potassium hydroxide bulbs. The result of this experiment was simply carbonic acid, the increase in weight of the drying tubes being only 0.0009 gram.
This led to the conclusion that the mass left by the ether and chloroform was simply carbon, in the form of soot. The 100 c.c. for the estimation of pyrohigeneous and empymomatic oils and pyridin was treated with pure, strong sodium hydrobide, and calcium oxide, placed in a glass retort, and kept at a temperature of 60° C. for three hours, the neck of the retort being connected with a flask containing a normal solution of sulphuric acid in such a manner that all the vapor coming from the retort must pass through the solution. The amount of sulphuric acid neutralized by the alkali in the vapor was 0.439 percent of alkali. 117 As all the alkaloids in tobacco smoke are supposed to be non-volatile at a temperature of 60° C. the neutralizing agent was taken to be ammonia and estimated as such.
Upon adding acetic acid and platinic chloride to the solution no precipitate occurred, which indicated that there was no nicotine present.

Emulsionation. Pyrogallic oil.

The original solution, still containing the ammonia and calcium hydroxide, was shaken up with four ounces of pure ether, the ethereal solution decanted, and the ether removed by evaporation. The residue was then digested with pure water at 60° C. for four hours, and the water removed by decantation. Res. A. Sol. B.

The water solution was then evaporated to dryness and the residue weighed. Weight 1.9300 lb.

This was taken as the weight of pyridine, nicotine, and all the other alkaloid soluble in water. The weight of nicotine previously found was subtracted from this weight and
the remainder estimated as pyridine and other alkaloids of smoke not precipitable by Pt Cl₄ in NH₄ H₂ O₂ solution.

The residue A was dried at 100°C. for three hours and weighed and estimated as empyromastic and pyroligneous oils.

Hydrocyanic Acid.

From the 50 C.C. reserved for general qualitative work 1 C.C. was placed in a watch glass, and another watch glass having upon its concave surface a drop of silver nitrate was inverted over it. According to Wormley, 1/10 of a grain of hydrocyanic acid will give a very marked precipitate when thus treated, but in this case not the slightest trace of turbidity appeared. The conclusion was, therefore, that if any hydrocyanic acid existed in the smoke it was in very minute quantities, less than 1/100 of a grain per cubic centimeter of the solution used.
In order to determine the amount of carbonic acid, carbonic oxide, an ordinary test tube was placed in connection with the pipe and the Bunsen pump and the smoke allowed to pass through it until all the air was expelled, when the connection was broken and the smoke in the tube transferred as rapidly as possible to an eudiometer which had been previously filled with mercury and inverted in a trough of mercury. As soon as the eudiometer had acquired the temperature of the surrounding air readings were taken by means of a cathetometer, the eudiometer, barometer, trough and thermometer. A stick of potassium hydroxide was then admitted to the smoke by means of a long platinum wire. At the end of twenty-four hours the KOH was drawn beneath the surface of the mercury in the eudiometer and readings taken.
The volumes were then reduced to 0° C. and 740 mm. of mercury pressure, by Bunsen's formula. The difference between these two volumes represents the volume of carbonic acid and water, which equaled 8.1374 per cent. of the smoke used. Subsequently a similar portion of smoke was dried over sulphuric acid and the volume of water found. Per cent of water 1.1714 which, being subtracted from the next preceding number gave 6.9650 as the per cent. of carbonic acid. Pure oxygen was then admitted to the tube and an explosion produced by means of a spark from an induction coil, and readings again taken. Per cent of carbonic oxide found 97.13

Specimens of Durham and Little Jockeyskin tobacco were also analyzed. Collecting the results of the investigations we find that the products separated occur in the following quantities referred to as tobacco used.

\[ 3 \times 10^{-5} \]
<table>
<thead>
<tr>
<th></th>
<th>Native grown</th>
<th>Durham</th>
<th>Little Jokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine</td>
<td>.7314</td>
<td>.1132</td>
<td>Traces</td>
</tr>
<tr>
<td>Pyridin</td>
<td>4.0234</td>
<td>7.9128</td>
<td>5.3180</td>
</tr>
<tr>
<td>Ammonia</td>
<td>1.1170</td>
<td>1.3807</td>
<td>1.2794</td>
</tr>
<tr>
<td>Carbonic Acid</td>
<td>6.9690</td>
<td>8.2381</td>
<td>4.1484</td>
</tr>
<tr>
<td>Carbonic Oxide</td>
<td>.9713</td>
<td>.0173</td>
<td>Traces</td>
</tr>
<tr>
<td>Oils</td>
<td>2.1713</td>
<td>2.2440</td>
<td>2.1342</td>
</tr>
<tr>
<td>Carbon (free)</td>
<td>1.2211</td>
<td>.0743</td>
<td>1.1132</td>
</tr>
<tr>
<td>Resin</td>
<td>3.7198</td>
<td>2.8370</td>
<td>2.1574</td>
</tr>
<tr>
<td>Prussic Acid</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Water</td>
<td>1.1714</td>
<td>.8214</td>
<td>2.1783</td>
</tr>
</tbody>
</table>

No reliance whatever can be placed upon the percent of carbonic acid and carbonic oxide contained in a specimen of smoke, as the rapidity of the draft to which the tobacco is subjected, while burning causes enormous fluctuations in the amount.
Nicotine is a light oily base having the formula \(C_{10}H_{14}N_2\). The pure alkaloid is of a faintly red color, rapidly changing to bright red upon exposure to the air, especially upon the application of heat. The enclosed photographs represent a specimen of nicotine obtained from "Little Joker" smoking tobacco, precipitated with platinic chloride.
Nicotine has a specific gravity of and vapor density of. It boils at 80°C, evolving dense white fumes of an extremely suffocating nature. The pure alkaloid is a most intense and rapid poison, animals having been frequently killed, during these experiments by the hypodermic injection of a single drop. The poison appears to act directly upon the nerves, in a manner analogous to strychnine and brucine. The animals experimented upon seldom survived more than five minutes, all dying in violent convulsions.

Double Salts.

Upon the addition of mercuric chloride, nicotine gives a white amorphous precipitate of the double chloride of nicotine and mercury. Half a gram of this salt, after being thoroughly washed to expel possible traces of the free alkaloid, was
administered to a large terrier dog, by the mouth. At the end of thirty-five minutes violent symptoms began to manifest themselves, but after vomiting some twenty times the animal entirely recovered. The same experiment was subsequently tried upon the same animal, except that platinic chloride was used in precipitating the alkaloid instead of mercuric chloride. No violent symptoms appeared. Nicotine in this form, like cyanogen in ferric ferrocyanide, seems to be insoluble, hence most injurious.

Antidote for anaesthesia.

The most noticeable feature in the experiment on the animals was the wonderful effect of nicotine on the organs of respiration and circulation. In several cases chloroform was administered until both respiration and circulation appeared to have
entirely ceased, when a very small drop of nicotine was placed in a hypodermic syringe with a few drops of water, and injected into the fleshy part of a leg, when rapid and violent breathing at once commenced, and continued until the animal completely recovered. The same result was obtained when ether was used.

When the quantity of nicotine used was sufficient to produce violent symptoms, platinic chloride was injected into a vein, when the symptoms soon ceased, and the animal completely recovered.

Pyridine is never present in tobacco itself, but is always present in the smoke from all kinds of tobacco, from the strongest to the weakest. It belongs to the most prevalent hydro-carbon nucleo $C_6H_5 \text{CON}$ It was first obtained from oily products on dry distillation of coal, peat, & bones. It has also been prepared from compounds of the group.
It may also be obtained in small quantities by the action of phosphoric anhydride on ionic nitrate—thus: \( \text{C}_6\text{H}_5\text{ONO}_2 + 3\text{P}_2\text{O}_5 = \text{C}_6\text{H}_3\text{PO}_4 + 6\text{H}_2\text{O} \).

It is a colorless liquid, having a sharp, nauseating odor, boils at 114.5°C. Specific gravity 0.984 at 0°C. It forms a yellow precipitate with platinic chloride, difficultly soluble in water.

**Picoline.**

This compound has the formula \( \text{C}_6\text{H}_5\text{N} \), and is formed by the dry distillation of acrolein with ammonia. Thus: \( \text{C}_6\text{H}_5\text{NO} + \text{H}_2\text{O} = \text{C}_6\text{H}_5\text{N} + \text{H}_2\text{O} \). Also by heating glycerol tribromide to 250°C with alcoholic ammonia.

It is a strongly basic liquid, closely resembling nicotine and pyridine. Very soluble in water, boils at 135°C. Sp. gr. 0.941 at 0°C.

**Collidine.**

Formulas \( \text{C}_8\text{H}_{11}\text{N} \). Is formed from aldehyde ammonia...
by dry distillation or heating an alcoholic solution to
120°-130° C.

Lutidine

Very little is known of this body. It is only obtained
from tar, oil, and smoke.

Smoke. General effects.
The first effect of tobacco smoke upon the system of one
not accustomed to its use is extreme dizziness, frequently
accompanied by nausea and vomiting.
These effects are probably due to nicotine, and in very
rare cases become so violent as to produce death.
The secondary effects, trembling, shooting pains, and
a desire to sleep are probably due to the action of pyridine.
The carbonic acid contained in the smoke is not
supposed to be injurious. The carbonic oxide is a violent
poison if inhaled, but when absorbed by the papillae
of the tongue appears to produce no other effect than
"See Strecker's Wirz'seneus Organ, Chem., P. 518"
extreme thirst. The free carbon of the smoke blackens the teeth. Ammonia, and the pyrolineous oils produce a biting sensation in the tongue, especially after long smoking. There are many poisons which, after they have been taken into the system, a little at a time for a considerable period, finally appear to lose their power to produce their specific effects. This is true of all the poisons contained in tobacco smoke. It is not to be supposed from this, however, that a continual indulgence of the habit of smoking will entirely obliterate the evil effects of the practice. There are many cases of epilepsy, paralysis, and death which are doubtless justly attributable to this cause.

Conclusion.

1. Nicotine undoubtedly occurs in tobacco smoke!
2. But it is undoubtedly associated with other organic alkaloids resulting from its own decomposition or that
of other organic nitrogenous bodies associated with it in crude tobacco.

3. The alkaloids appear to be about equally poisonous, and about equally injurious to smokers, although some of them manifest their poisonous properties much more quickly than others.

4. Nicotine is always associated with ammonia in the smoke, and may be separated from it by precipitation with mercuric chloride, in the presence of acetic acid.

5. Very little if any good can possibly result from smoking, and great harm may ensue.