CARBONIC OXIDE IN TOBACCO SMOKE.

BY

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WHEN recently the carbonic oxide scare was raised in the press, the danger we incur, even in the streets, from the constant discharge of the exhaust gas from bus and motor-car engines was a matter of scarcely joking comment. Some of us, knowing the secrets of combustion, were moved to suggest to tobacco-using friends that they were risky companions. The subject of cigarette smoking was discussed in these columns in November last* by my friend Professor W. E. Dixon, F.R.S. I learn from him that he has regarded the pernicious result of excessive cigarette smoking as an effect of carbonic oxide but that he is inclined to attribute the obvious effects of cigar smoking rather to the influence of nicotine, if not to other basic products of the destructive distillation of the noxious weed.

Apparently the gases from the burning cigar have not been specially examined for carbonic oxide. Discussing the matter with my neighbour, Mr. E. V. Evans, chief chemist to the South Metropolitan Gas Company, we came to the conclusion that it was worth while for once to make a few experiments on combustion of a practical character, to ascertain the extent to which poison-gas manufacture is indulged in by the public; at his invitation I have participated in the work. We advisedly do not call it a research, as the results are sufficiently striking to be of public interest and the work has been done without Government grant.

Sulphuretted hydrogen and prussic acid are both constant products of the smoker's activity, though in very minute proportions. This is easily demonstrated by smoking a cigarette in a glass-tube-holder into which a strip of test paper is first inserted, then a close plug of cotton-wool and finally the cigarette. Acetate of lead paper is blackened after a few whiffs; similarly, after removal of sulphuretted hydrogen, a paper impregnated with a solution of orthotoluidine in cupric acetate and water—a most delicate test for hydrogen cyanide—rapidly turns blue. The less sensitive picrate and Prussian-blue tests are more slowly effective.

The blood test for carbonic oxide, in our experience, cannot be applied effectively to smoke—something is present which mars the colour change; it can only be used after scrubbing the smoke by means of cotton-wool, fuming sulphuric acid and a concentrated solution of caustic soda.

The following results were obtained by smoking a cigarette or pipe, by attaching it to a gas-sampling bottle and allowing mercury to run out in "puffs."

	"Gold Flake."	"Player's Weights."	"Sylvion" (Virginian).	"Medium Shag" in Pipe.
CO ₂	4.50	7.02	4.25	10.15
CO	0.89	1.24	0.97	1.14
O ₂	16.20	15.60	16.54	10.53

The oxygen may be taken as a measure of the excess air. Multiplying the values by 5, it appears that about 80 per cent. of air in excess was drawn through the cigarette and only about 50 per cent. through the pipe.

* BRITISH MEDICAL JOURNAL, November 19th, 1921, p. 819 et seq.

A cigar smoked in a similar way gave the following most surprising figures:—

CO ₂	...	...	...	...	13.36 per cent.
CO	...	...	...	...	5.8
O ₂	...	...	...	...	5.8

The amount of air in excess was under 30 per cent., showing that the cigar is a very efficient instrument. Both the amount and the high ratio of carbon monoxide to dioxide

$$\frac{13.36}{5.8} = 2.3$$

are remarkable.

In these experiments the gases were analysed directly in a Bone and Wheeler apparatus. The percentage of monoxide being so small from the cigarette, we deemed it advisable to use Gautier's perhaps more trustworthy method (for small amounts), in which the purified gas is passed over heated iodine pentoxide, the iodine liberated in oxidizing the carbon monoxide being determined by titration. To ascertain the effect of smoking more or less rapidly, the rate at which mercury was run out was varied considerably. The percentages of carbonic oxide thus estimated came out as follows:

1. Turkish cigarette (smoked normally)	...	CO	0.72
2. Virginian cigarette (smoked normally)	...	CO	0.673
" " " " " "	...	CO	0.714
" " " " " "	...	CO	0.78
3. "Wild Woodbine" cigarette (smoked slowly)	...	CO	0.6
" " " " " " (smoked normally)	...	CO	0.875
" " " " " " (smoked quickly)	...	CO	1.40
4. "Three Nuns" tobacco (bowl of pipe cool, sampled shortly after lighting up)	...	CO	1.14
5. Player's "Tawny" (pipe; beginning of smoke)	...	CO	0.9
" " " " " "	...	CO	0.7
6. Havana cigar (smoked quickly)	...	CO	8.13
" " " " " "	...	CO	6.0

It is clear from these results that the proportion of carbonic oxide in the smoke will vary according to the rate of smoking. When air is drawn in rapidly the length and temperature of the glowing portion are increased and more of the monoxide is formed. In general, however, a normal sample of cigarette smoke will contain between 0.5 and 1 per cent. of carbon monoxide.

In all these trials the smoking was artificial. In a final series cigars were smoked in the usual manner but the smoke drawn into the mouth was afterwards expelled into a mercury receiver and then analysed. The cigars used were a set specially selected for me by a friend who is a maker. The results in column A of the following table apply to smoke obtained by mercury suction; those in column B represent the effect of normal smoking. X is the ratio of dioxide to monoxide. The high proportion of air in two cases in the B series is to be ascribed, we think, to the mouth not fitting the cigar (a big one) closely. It will be noticed that, in the A series, the old, well-matured cigar seems to have offered a specially free passage to air and that this gave the lowest proportion of carbonic oxide. The irregularities in the results need not be taken too seriously, being doubtless in the main due to the irregular character of the operation of smoking as it was practised in these trials.

Apparently the results are little affected by make or quality; closeness of packing and rate of smoking seem to be the determining factors. In the A series the cigar was only smouldering; in the B series the length of the burning portion was greater and the proportion of monoxide is usually higher. It would seem that the "strong" smoker produces

Comparison of Cigars of Different Quality.

Brand.	Quality.	Age.	Moisture.	A.				B.			
				CO.	CO ₂ .	O ₂ .	X.	CO.	CO ₂ .	O ₂ .	X.
			Per cent.	Per cent.	Per cent.	Per cent.		Per cent.	Per cent.	Per cent.	
British ...	Good	Quite new	8.86	2.31	16.4	4.3	7.1	5.69	14.4	4.4	2.5
British ...	Fairly good	Quite new	11.60	2.65	15.7	4.3	6.0	7.93	14.3	4.4	1.8
British ...	Fair	Somewhat aged	9.52	1.86	9.0	7.9	4.9	5.26	13.5	4.2	2.3
British ...	Common	Fairly old	10.97	2.44	10.2	7.6	4.2	2.23	6.0	11.7	2.7
British ...	High class	Old and well-matured	9.80	1.25	5.5	11.4	4.4	2.54	6.6	11.6	2.2
Havana ...	Fairly good	Old	9.77	2.81	9.2	5.5	3.2	5.43	10.5	6.5	1.9
Havana ...	Medium	Old	8.33	4.96	13.9	4.2	2.8	4.52	7.7	8.0	1.7
Havana ...	High class	Old	9.28	2.65	14.7	4.4	5.5	3.91	9.9	7.3	2.6

the greater amount of carbonic oxide by maintaining a longer layer of the cigar red-hot.

It is of interest to compare the proportions of carbonic oxide in straight coal gas, made by simply distilling coal, with that in tobacco smoke.

A cigar of average size was smoked under such conditions that the volume of smoke formed could be measured. Four-fifths only of the cigar was smoked in order to make allowance for the portion of cigar usually discarded. It was found that 0.303 cubic foot of smoke was produced, of which 7 per cent. was carbonic oxide. The quantity of straight coal gas containing an equivalent amount of carbonic oxide is 0.25 cubic foot—that is, 1 cubic foot of straight coal gas contains an amount of carbonic oxide equal to that in the smoke from four cigars; the proportion of carbonic oxide in South Metropolitan gas, it may be added, is about that of average cigar smoke.

As to the effects of smoke, the cigarette smoker often has the habit of inhaling; but as a rule pipe and cigar smokers do not; friends tell me that pipe and cigar smoke are nauseous when inhaled: apparently volatile products of distillation are carried forward much more than in cigarette smoking and these protect the cigar smoker notwithstanding the larger production of carbonic oxide. The blood of the cigarette smoker often shows signs of carbonic oxide absorption. A friend, who is an excessive smoker, is said to have 5 per cent. of his blood out of action; another who is an equally great smoker and inhales constantly shows no sign of absorption. The latter is an exceptionally vigorous person, who eats and drinks freely; apparently his is scarcely a case of tolerance: if carbonic oxide enter his blood either it is swept out without difficulty by gaseous exchange or is worked up in some way. Apparently there is room for further study of the conditions regulating the natural exchange of carbonic oxide for oxygen in the blood. Smoking has its interesting side, even for the non-smoker.

We have to thank Mr. Pickard and Miss Bucknell for the very skilful aid they have given and the special interest they have taken in this little experimental excursion.

OBSERVATIONS ON THE AMOEBICIDAL ACTION OF CONESSINE.

BY

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THE bark and seeds of *Ho'arrhena antidysenterica* have been held to rank amongst the most important medicines of the Hindu materia medica for many centuries; in fact Garcia de Orta, who wrote in 1563, speaks of their great merit in the treatment of dysentery. The plant is a small deciduous tree found throughout India and Burma, belonging to the Apocynaceae; according to Sir George Watt,¹ it has been confused with another species, *Wrightia tinctoria*, belonging to the same family.

From *Wrightia antidysenterica*, Stenhouse,² in 1864, isolated an amorphous base forming amorphous salts. Hains³ had previously obtained the same alkaloid and described it under the name of "conessine."

The alkaloid conessine is now a commercial product prepared by Merck, and the formula $C_{15}H_{20}N$ is given to it. In the United States *Dispensatory*, nineteenth edition, it is stated that the medicinal properties of this substance have apparently not been investigated.

In 1880 Baboo Rakhal Das Ghose⁴ described *Holarrhena antidysenterica* (Wall) as being synonymous with *Wrightia antidysenterica*, and from the seeds he obtained an alkaloid, which was isolated by Baboo Ram Chandra Datta, which the latter called "kurchicine." He found it useful in cases of chronic dysentery, and used it in doses of 2 to 5 grains.

Burn⁵ gives an account of the physiological action of conessine, holarrhene, and oxyconessine, and Pyman⁶ in 1919 described the chemical properties of holarrhenine and conessine. Apart from the study of the physiological action of the alkaloid by Burn no attempt has apparently been made to study the action upon the causative agents in dysentery.

The remedy is chiefly used in Northern India in the form of an infusion of kurchi, this being the Bengali name for the plant. The efficacy of this infusion in certain cases of dysentery is, in the opinion of those who have used it, little short of miraculous, and it seems strange that although

conessine has been isolated for more than half a century the amoebicidal action of this drug has apparently not been tested. I have seen two cases in which its effect was very striking, in one of them dramatic. It may be that, as Burn pointed out, although the alkaloid possesses the properties of a local anaesthetic it cannot be used as such, at any rate by the hypodermic route, owing to the production of a necrotic area at the site of the inoculation; the necrosis is apparently quite independent of secondary contaminating organisms and is produced even with doses of 10 milligrams.

The preparation with which the following experiments were made was in the form of a neutral solution of conessine sulphate, originally isolated by Dr. Pyman from a sample of *Holarrhena congolensis* obtained from the Belgian Congo; a regular supply has been sent to me through the kindness of Dr. Henry, Director of the Wellcome Chemical Research Laboratories.

In the first place an attempt was made to ascertain whether the alkaloid had any specific bactericidal action on bacilli of the dysentery group. It was found that although the drug did exert some specific action *in vitro* such large doses had to be used as to place any chance of cure of bacillary dysentery by this means outside the bounds of probability, and the rest of the investigation was directed to the action of conessine upon the growth of amoebae.

As it was not found possible to obtain suitable material from an acute case of amoebic dysentery with which kittens might have been infected and the strain maintained, the action of the alkaloid was studied upon cultures of free-living amoebae which had been isolated from pond water by Dr. Wenyon; for these cultures, and for his valuable suggestions and guidance, I wish to express my best thanks. The cultures of this strain of amoebae were maintained upon an agar medium (Walker's medium) upon which the amoebae grew luxuriantly at room temperature.

There is a great deal of discrepancy in the published statements as to the results obtained by different observers when studying the amoebicidal action of emetine upon material from the intestinal contents in which *Entamoeba histolytica* was present. For instance, Leonard Rogers⁷ states that when a small piece of mucus containing these active amoebae was placed in saline solutions of emetine of the strength of 1 in 10,000 the organism was immediately killed, and that even in a 1 in 100,000 dilution they were rendered inactive and apparently killed after only a few minutes' immersion. Dale and Dobell,⁸ however, found that certain of their strains of *Entamoeba histolytica* survived the action of 1 in 1,000, and even 1 in 100 emetine for periods up to one hour. Further, Wenyon and O'Connor⁹ showed that amoebae in pus treated with a 6.5 per cent. solution of emetine could remain alive for several minutes.

Of course it is not possible to say that the conditions of the test in each case were exactly comparable, and it appears that the relative differences in the amount of intestinal mucus present may be a variable factor in the experiments. This intestinal mucus is capable of interfering with the action of emetine, as is shown in the following experiments.

Experiment I.

A 1 per cent. solution of conessine sulphate and a 1 per cent. solution of emetine hydrochloride were made. Of these 5 c.cm. was placed in two small centrifuge tubes, then to each tube an equal amount of intestinal mucus was added, the quantity of mucus being approximately 1 c.cm. The mucus was then beaten up for five minutes and the tubes centrifuged for five minutes. From the supernatant fluid varying dilutions were made and then 1 c.cm. of these dilutions was added to 9 c.cm. of the melted agar. These tubes were then autoclaved, the contents poured into Petri dishes, and the surfaces planted with a saline suspension of amoebae.

Emetine Hydrochloride concentration in the Medium.	Bacterial Growth.	Amoebic Growth.	Conessine Sulphate concentration in the Medium.	Bacterial Growth.	Amoebic Growth.	Control.
0.1 %	++	0	0.1 %	++	0	
0.01 %	++	0	0.01 %	++	0	Bacterial growth } ++
0.001 %	++	++	0.001 %	++	+	Amoebic growth } ++
0.0001 %	++	++	0.0001 %	++	++	

Experiment II.

This experiment was repeated as above, only in this case a four hours' contact was allowed between the mucus and the reagents, with the result shown in the following table.