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On the Acute Toxicities of the Combustion Products of Various Fibers, with Special Reference to Blood Cyanide and Po_2 Values

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Summary. The blood cyanide and Po_2 levels in different parts of the body were determined in the rabbit exposed to HCN.

After urethane anesthesia, the rabbit was made to inhale HCN gas through a tracheal cannula. In addition to pure HCN gas produced by addition of NaCN to H_2SO_4, the combustion products from PAN (polyacrylonitrile), silk and wool were used respectively. After ultimate cessation of respiration, the chest was opened and the blood samples were taken from the three places, the left and right heart (ventricles) and the descending vena cava and cyanide and Po_2 values were determined.

The survival time was the shortest in PAN group among the combustion experiments. Silk group followed it. The decreasing order of the blood cyanide levels was silk, PAN, HCN and wool groups with respect to all sampling sites. There was not significant difference in cyanide levels among silk, PAN and HCN groups. The left heart showed the highest cyanide values of all the sampling places. Significant positive correlation was present between postmortem cyanide and Po_2 values. Inhalation of relatively large amount of HCN and the concomitant inability of cardiac function to maintain the systemic circulation effectively at the last stage were considered to contribute largely to the unequal distribution of cyanide with the highest level in the left heart blood.

Key words: Combustion products of fibers – Toxicity of combustion products – Blood cyanide values – Blood-Po_2-values.

Zusammenfassung. Die Blutzyanidkonzentrationen und der Po_2 in verschiedenen Körperteilen von Kaninchen wurden in experimentellen inhalatorsichen HCN-Vergiftungen bestimmt.

Die mit dem Urethan narkotisierten Kaninchen wurden HCN durch Trachealkanülen bis zum Atemstillstand ausgesetzt. Außer reiner Blausäure, die von NaCN und H_2SO_4 entwickelt wurde, wurden die Verbrennungsgase von stickstoffhaltigen Fasermaterialien (Polyacrylonitril [PAN], Seide und Wolle) gebraucht. Nach endgültigem Atemstillstand, wurde die Brust geöffnet und die Blutproben

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wurden von 3 Orten, den rechten und linken Herzventrikeln und der kaudalen Hohlvene entnommen. Außer der Zyanidkonzentration, wurde der Po_2 des Blutes gemessen.
Die Zeitdauer bis zum endgültigen Atemstillstand war am kürzesten in der PAN Gruppe von den Verbrennungsversuchen. Die Seidegruppen folgte ihr. Die Blutzyanidwerte zeigten die folgende Reihenfolge; Seide > PAN > HCN > Wolle. Der Unterschied zwischen Seide, PAN und HCNgruppen war statistisch nicht signifikant. Der linke Ventrikel zeigte den höchsten Blutzyanidwert von den untersuchten 3 Orten. Es gab positive Korrelationen zwischen Po_2 und Zyanid. Es wurde angenommen, daß die Inhalation von verhältnismäßig größerer Menge von Blausäure in den agonalen Perioden und die gleichzeitige Unmöglichkeit des Herzens, den Allgemeinkreislauf erfolgreich zu erhalten, zu der ungleichen Zyanidverteilung mit dem höchsten Wert im linken Ventrikel beitrug.

Schlüsselwörter: Schwelprodukte von Fasern – Toxizität von Schwelprodukten – Blut-Cyanid-Werte – Blut-Po_2-Werte.

The evaluation method of the toxicities of various materials at fires and the studies on the harmful effects of various combustion products are considered to be the main subjects in the toxicology on combustion. The present report chiefly concernes with the second item. The combustion toxicology generally deals with the gaseous form, therefore, inhalation route is the main entrance route of the toxicants into the bodies. There can be marked difference in concentrations and in distribution patterns of the toxic materials in the body with different routes of administration. That the above can hold true for cyanide too was indicated in the author's previous preliminary experiments with rats and rabbits, in which two routes of administration, per os and inhalation routes, were used and the blood cyanide levels were compared between the left and the right sides of the heart [1].

Since there is only a limited number of data on the distribution of cyanide in the body exposed to HCN gas [1, 2, 3, 4, 5, 6], it seemed to be worthwhile, as a first step to obtain such basic data, to determine the blood cyanide concentrations in the different parts of the body. The present report includes the data on blood Po_2 level as well as cyanide. This is based on the following considerations that this parameter can be used for a diagnosis, whether death is an asphyxial one or not, and that Po_2 can give some clue to the problem of identity of the gases responsible for the toxic effects of the combustion products.

Materials and Methods

Materials. Polyacrylonitrile (PAN), silk, wool and gauze were used for combustion experiments. The first three were obtained from Nippon-Boen-Kyokai and gauze (the Japanese pharmacopoeia) was purchased. The each material was cut to pieces of about 1.5 cm square. Twenty gram of material was used in the experiments with the first three. In the case of Gauze, 20 g and 30 g were used in Exp. Nos. 1–4 (see Tab. 1) and in Exp. No 5, respectively.

Experimental Apparatus and Conditions. They were virtually the same as those of the previous experiments [7] except slight modifications and only brief account is given here as follows. The sample was heated in a cylindrical mesh cage of stainless steel with an electric heater of 300 w in a plastic combustion room measuring 30x30x50 cm. The combustion product was lead through

Table 1. Experimental results. Rabbits anesthetized with urethane were exposed to HCN or combustion gas until cessation of respiration. When respiration stopped ultimately, the chest was opened and the blood samples were taken from three places (L: the left heart, R: the right heart, V: the descening vena cava), respectively, for determination of cyanide and Po_2

			Cyanide (μg/ml)			Po_2 (mmHg)		
Materials	Exp. No.	ST (min)	L	R	V	L	R	V
HCN inhalation	1	4.8	5.53	3.30		54	33	
	2	9.9	4.42	2.71	1.83	51	32	23
	3	14.0	1.24	1.04	0.88	19	11	9
	4	7.3	3.64	2.35	1.72	37	26	18
	5	11.1	3.72	2.18	2.03	80	20	16
	6	6.4	1.94	1.58	1.44	19	7	7
PAN	1	16.5	8.14	3.54	3.14	75	30	28
	2	14.1	1.55	1.47	1.34	12	6	6
	3	15.4	1.99	1.66	1.56	22	15	11
	4	16.6	1.49	1.44		19	13	
	5	11.2	2.92	1.93	1.37	40	17	16
	6	13.6	3.87	2.36	1.75	61	32	19
	7	13.2	2.81	2.01	1.64	46	37	28
	8	11.4	8.55	4.12	2.77	105	52	41
Silk	1	17.2	5.37	3.81	2.30	47	25	13
	2	16.7	3.18	1.97	1.48	28	18	16
	3	16.5	5.22	2.96	1.49	102	35	18
	4	15.5	4.31	3.03	2.05	57	29	17
	5	14.9	5.40	3.11	2.31	76	36	26
	6	16.4	5.96	2.79	1.63	98	42	29
	7	19.4	1.31	1.12	1.07	23	20	19
	8	17.3	5.91	3.52	2.53	104	39	34
Wool	1	25.1	0.11	0.11	0.09	3	4	4
	2	15.0	0.10	0.07	0.05	65	46	14
	3	31.8	0.13	0.13	0.12	9	4	5
	4	16.0	0.08	0.06	0.05	10	7	4
	5	50.0	0.39	0.29	0.29	44	16	16
	6	15.2	0.09	0.06		41	20	
			COHb (%)					
Gauze	1	33.0		86	84		5	3
	2	32.2	84	88	86	35	6	6
	3	survived	59	65	65	5	4	3
	4	survived	56	52	52	9	7	4
	5	survived	63	60	59	13	13	12

a 50 cm-long plastic tube to a transparent plastic box which was used as an exposure room, to which a non-rebreathing valve was attached via a short piece of a plastic tube.

HCN Inhalation Experiment. HCN was produced by addition of NaCN to H_2SO_4. To H_2SO_4 in a flat-bottomed flask, the diameter of and the height of which are 26 cm and 36 cm, respectively, with a perforated rubber stopper, solid NaCN was added at proper intervals through one of the perforations. The rate of addition of NaCN was not fixed and it was changed during exposure, depending upon the state of the animal. Into the other perforation a glass tube with a diameter of 0.7 cm was inserted and it was connected to the non-rebreathing valve by a short plastic tube.

Animals. Male albino rabbits each weighing about 2,000 g were used. After intravenous urethane injection (1 g/kg, 25 % in saline), the animal was fixed supinely and a tracheal cannula was inserted following tracheotomy. The animal inhaled the gas of the exposure room (in combustion experiment) or HCN gas (in HCN experiments) through the non-rebreathing valve attached to the cannula. Combustion experiments were continued until ultimate cessation of respiratory movement of the chest, however, when respiration did not stop during 50-min exposure, the experiment was discontinued at that time. Immediately after the end of an experiment, the chest was opened and blood sample was drawn from the left heart, the right heart and the descending vena cava, respectively, in this order. The blood sample was stored in ice until determination, the start of which did not delay more than 30 min after sampling in the cases of cyanide and Po_2.

Toxicological Determinations. The whole blood cyanide determination was made by the method of Feldstein et al [8], triplicate determinations being done on each sample. COHb saturation was determined spectrophotometrically by van Kampen et al's method [9]. Before exposure, small amount of jugular vein blood was taken from each animal, and it was used for a preparation of the calibration curve. Blood Po_2 was determined by Combianalyzer U. Prior to each analysis, the instrument was calibrated with standard gases. The O_2 concentration in the exposure room was continuously determined by Beckman O_2 analyzer. The respiratory rate of the animal was measured by counting the frequency of the movement of the chest per unit time. After combustion experiments, in some cases, the lung was excised and fixed in formalin solution for subsequent hematoxylin-eosin staining. The residual ash was weighed after each experiment and the vapoured ratio (%) was calculated according to the following equation,

$$\left(1 - \frac{\text{ash weight}}{\text{original weight}}\right) \text{x } 100$$

Results

Survival time (ST, the time to ultimate cessation of respiration), blood cyanide, Po_2 and COHb values are shown in Table 1. Table 2 gives the summarized data.

HCN Inhalation. The ST ranged 5–14 min. The cyanide concentration in the left heart blood averaged 3.4 μg/ml, ranging from 1.24–5.53 μg/ml. The mean value and range of the right heart blood were 2.2 μg/ml and 1.04–3.3 μg/ml, respectively. The corresponding values of the blood in the descending vena cava were 1.6 μg/ml and 0.88–2.03 g/ml, respectively. The ratio of the left heart to the right heart value was 1.2–1.7. The ranges and means (given in the bracket) of the blood Po_2 of the left heart, the right heart and the descending vena cava were 19–80 mmHg (43 mmHg), 7–33 mmHg (22 mmHg) and 7–23 mmHg (15 mmHg), respectively. The decreasing order of the Po_2 was identical with that of the cyanide concentration. The rabbit with high postmortem cyanide value showed high Po_2 value. The six animals in the present report could be divided into two subgroups, based on the magnitude of the blood Po_2 and cyanide values, one group consisting of 4 animals (Exp. Nos. 1, 2, 4, 5) with high cyanide and Po_2 values and the other one with low in the both.

PAN. All the animals were killed during exposure and the range of the ST were 11–17 min. As in the HCN experiment, the left heart blood showed the highest cyanide value. The next highest concentration was recorded in the right heart blood. The decreasing order of the cyanide concentration was the same as that of the HCN experiment. The same relation as that in the HCN experiment was present between cyanide and Po_2 values. The concentration of COHb was very low. There was neither soot nor froth in the trachea macroscopically.

Silk. None of the animals survived exposure and the ST was significantly longer in this group than in PAN group. The respiration during exposure was comparatively

Table 2. Summarized results. The data were expressed in terms of mean ± s. d. with the numbers of the animals in bracket

Materials	ST (min)	Cyanide (μg/ml) L	R	V	Po_2 (mmHg) L	R	V
HCN inhalation		3.4 ± 1.6(6)	2.2 ± 0.8(6)	1.6 ± 0.4 (5)	43 ± 23(6)	22 ± 11(6)	15 ± 7(5)
PAN	14.0 ± 2.1(8)	3.9 ± 2.8(8)	2.3 ± 1.0(8)	1.9 ± 0.7(7)	43 ± 30(8)	25 ± 14(8)	21 ± 12(7)
Silk	16.7 ± 1.3(8)	4.6 ± 1.6(8)	2.8 ± 0.9(8)	1.9 ± 0.5(8)	67 ± 33(8)	31 ± 9(8)	22 ± 7(8)
Wool	21.9 ± 14(6)	0.2 ± 0.1(6)	0.1 ± 0.1(6)	0.1 ± 0.1(5)	29 ± 25(6)	16 ± 16(6)	9 ± 6(5)
Gauze					16 ± 13(4)	7 ± 4(5)	6 ± 4(5)

similar in PAN and silk groups. The respiratory rate began to increase with inhalation of the combustion gas. After peak, it began to decrease again, resulting in temporary apneic state in almost animals. At the last stage, gasping-like breathing prevailed, the magnitude of which varied from case to case. The mean blood cyanide concentration of the left heart, the right heart and the descending vena cava were 4.6, 2.8 and 1.9 μg/ml, respectively. This group showed the highest cyanide concentration of all the groups. The difference was the greatest in the left heart blood, but the difference among HCN, PAN and silk groups was not significant. As to the Po_2 value too, the silk group was the highest. As in the preceding two groups, the animal with high postmortem Po_2 value showed high cyanide value. The COHb level did not exceed 10 %. In 6 out of 8 animals, froth was present in the upper respiratory tract, on the other hand, not any soot was macroscopically observed.

Wool. All animals died during exposure. The ST ranged 15–50 min. In this group cyanide concentration was very low compared with PAN and silk groups. On the other hand the COHb concentration was about the same as that in silk group. There were present in some animals both soot and froth in the trachea.

Gauze. Only 2 out of 5 animals succumbed during exposure. The time were 32 and 33 min, respectively. The other 3 animals showed severe respiratory depression after about 25–40 min's exposure, but thereafter, showed the tendency to restore. The COHb levels were as high as 85 % in the animals died during exposure, on the other hand, the value ranged 55–65 % in animals survived exposure. Black particles were observed in the trachea in 1 died and 2 survived out of 5 animals, but no froth was observed.

Microscopically, in any group there was not marked change in the lung examined.

The correlation coefficients between postmortem blood cyanide and Po_2 values were calculated with respect to the pooled data from HCN, PAN and silk groups. The values for the left heart, the right heart and the descending vena cava, the number of respective data being given in bracket, were 0.84(22), 0.79(22) and 0.61(20), respectively. They were all statistically significant. The difference among the sampling sites was not significant.

The decrease of the exposure room O_2 concentration was not marked in experiments except that with gauze, the minimal concentration in which was 11–14 %.

The vapoured ratios differed from material to material. The mean values of gauze, wool, silk and PAN were 96, 68, 54 and 27 %, respectively.

Discussion

PAN and silk were considered more dangerous materials at fires than wool and gauze on the basis of the length of the ST and this result was consistent with the previous results [7], which showed the most dangerous material at fires to the PAN. As to identity of the gases responsible for hazard too, the present study agreed with the previous result [7]. HCN was the main toxic gas produced from PAN and silk. CO was responsible for the toxicity of the gases released from gauze.

There were considerable differences in both blood cyanide and Po_2 levels among different parts of the body. It is needless to say that to specify the source of the sample is very important in interpretation of the data [10]. The close relation between blood cyanide and Po_2 values indicates the great influence of the respiration at the last stage of the exposure on these values. The concomitant disturbance of cardiac function, which prevents newly inhaled HCN from being distributed effectively throughout the body, probably is the main cause of the concentration difference of cyanide among different parts of the body. The higher cyanide value in the right heart than in the descending vena cava is probably due to the diffusion of cyanide ion from the lung and/or the left heart.

The cause of the intragroup difference in cyanide level, which was relatively great in HCN and PAN groups, remains to be solved, and for a detailed discussion on this problem, the measurements of cardiac and respiratory functions such as blood pressure and ventilation, and quantitative evaluation on them will be indispensable. As in the previous experiment, silk group showed the highest cyanide values. The ratio of silk group to HCN group amounted to as high as 1.4 with the left hear blood. This seemingly puzzling data was considered to indicate that relatively large amount of HCN was inhaled in this group by gasping-like breathing immediately before ultimate cessation of respiration without being transported by the systemic circulation, for the difference in cyanide levels among HCN, PAN and silk was much smaller in the peripheral venous blood.

According to Mithoefer et al [11], irrespective of the source of the sample, the blood Po_2 above 25 mmHg is evidence against asphyxia as a cause of death. Since cyanide, in contrast to CO, inhibits the utilization of O_2 by tissue, the higher postmortem Po_2 is expected in acute cyanide poisoning than in acute CO poisoning. The way, by which cyanide is introduced into the body, seems to affect the Po_2 value. The Po_2 in gauze group was generally low in compared with those in HCN, PAN and silk groups with respect to the three kinds of the blood samples.

The cause of the hazard of wool at fires remained unknown in the present study. The cause of death is neither CO intoxication nor cyanide poisoning. From the Po_2 values it could not be concluded that the death is due to simple asphyxia.

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