The Effect of Habitual Smoking on White Blood Cell Count

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It would be widely accepted that leucocyte counts in healthy people range approximately from 4,000 through 9,000/mm^3.[1] In daily clinics, however, we often come across cases with the leucocyte counts well exceeding the range. Aside from clinical observations, about 3% of 12,000 and odd healthy Japanese were found having their leucocyte counts over 10,000/mm^3 in our previous studies.[2, 3] Most of them failed to show any trace of inflammation or any other clinical manifestations, making us puzzled about the reason.

We have studied cases with asymptomatic leucocytosis and found that it is closely related to habitual smoking.

Method

731 male workers with age between 15 and 60 years were studied. All of them, having underwent periodic health appraisals within a few months prior to out present study, were apparently healthy and had no contributory past histories. They comprised the following two groups; namely, 359 cases picked out as having their leucocyte counts over 10,000/mm^3, irrespective of smoking habits (group W), and 372 randomly picked up workers whose leucocyte counts were available. The latter group consisted of 179 nonsmokers (control group) and 193 habitual smokers (group S). The subjects so classified into the groups were further broken down by age categories as shown in Table 1.

Table 1. Number of Subjects

age	randomly selected		WBC > 10^4/mm^3		total
	non-smokers	smokers	smokers	non-smokers	
~ 29	47	44	67	7	165
30 ~ 39	63	63	145	7	278
40 ~ 49	40	41	76	3	160
50 ~	29	45	49	5	128
total	179	193	337	22	731

We did not deal with women because we failed to collect as many female smokers as would suffice our statistical study.

All subjects were those who had abstained from eating, drinking and smoking since around 10 p.m. until blood samples were taken on the following morning. Complete blood countings were done with an autohemocytometer, Coulter Counter Model SR. The rest of the most blood samples were then appropriated for blood smear, erythrocyte sedimentation rate, C-reactive protein, RA test, antistreptolysin O and liver function tests. In addition, all subjects were subjected to physical examinations along with urinalyses in order to get a wider scope for possible cause of leucocytosis.

Results

In the group W, 337 people who accounted for 93.9% of the group were found habitually smoking. The high percentage strongly suggested that leucocytosis was related to smoking, because the ratio of habitual smokers was as small as 58.0% in about 70,000 male worker population from which the subjects were extracted.

The means and the standard deviations of blood counts in each group are listed on Table 2. The mean leucocyte count for the group S was 7,094/mm^3, whereas 6,169/mm^3 was for the control group. The difference was statistically significant with the probability at 99%. Fig. 1, which illustrates

Table 2. Blood Measurements

	randomly selected		WBC > 10^4/mm^3	
	non-smokers	smokers	smokers	non-smokers
number	179	193	337	22
WBC x 10^2/mm^3	61.7 ± 12.92	70.9 ± 16.07**	115.2 ± 14.12	112.9 ± 13.71
RBC x 10^4/mm^3	493.3 ± 33.30	492.0 ± 33.04	504.9 ± 37.86**	498.5 ± 33.92
Hb. g/dl	15.1 ± 1.16	15.6 ± 1.10**	15.8 ± 1.17**	15.4 ± 1.10
Ht. %	44.5 ± 2.96	45.7 ± 3.02**	46.6 ± 3.26**	45.3 ± 2.98
MCH μμg	30.5 ± 1.93	31.7 ± 1.47**	31.3 ± 1.31**	30.9 ± 1.34
MCV c-μ	90.5 ± 4.53	92.9 ± 4.19**	92.2 ± 3.46**	91.0 ± 3.57
MCHC %	33.8 ± 1.08	34.1 ± 0.88**	33.9 ± 0.74	33.9 ± 0.55
number	77	88	210	12
Stab. %	3.4 ± 3.11	3.9 ± 3.13	4.2 ± 3.09	4.1 ± 3.53
Seg. %	49.2 ± 10.11	52.8 ± 9.45*	56.8 ± 10.66**	60.5 ± 8.52**
Baso. %	0.9 ± 1.14	0.8 ± 1.03	0.7 ± 0.86	1.0 ± 0.95
Eosino. %	3.1 ± 2.64	2.7 ± 2.43	2.3 ± 2.32**	2.2 ± 2.52
Lympho. %	41.6 ± 10.76	38.3 ± 8.94*	34.7 ± 10.13**	29.1 ± 7.20**
Mono. %	1.7 ± 1.83	1.5 ± 1.48	1.3 ± 1.44	3.1 ± 1.44*
number	168	184	225	16
ESR 1°mm	4.8 ± 4.99	4.6 ± 5.51	4.1 ± 3.84	5.6 ± 4.90
ESR 2°mm	12.5 ± 9.68	11.2 ± 10.32	10.9 ± 8.70	14.7 ± 12.79

* $P < 0.05$, ** $P < 0.01$
(t-test compaired with non-smokers)

the relative distributions of leucocyte counts in both groups, may well explain a considerable rightward shift of distribution on the part of the group S.

We further counted the number of each type of leucocyte in every subject, to see if any specific type(s) would be responsible for the leucocytosis. As shown in Table 3, all types but basophils in the smoker group with leucocytosis (group W-S) were significantly greater in number on the average than all corresponding types in the control group. Basophil counts were considered too small in both groups to be evaluated statistically. No type except segmented neutrophils in the group S, however, outnumbered significantly the same type in the control group. The failure would be due partly to relatively small difference in leucocyte counts between the two groups and partly to relatively big standard deviation in every type of leucocyte.

On the other hand, segmented neutrophils showed the most outstanding increase in the group W-S, but few cases among them had segmented neutrophils exceeding its upper normal percentile limit in the leucocyte count.

Accordingly, the leucocytosis seen among smokers can be regarded as brought about by overall upheaval in the number of every leucocyte type, not resulting from increase of any given type.

Fig. 2, 3 and 4, which illustrate the relative distributions of erythrocyte measurements in the group S, the group W-S and the control group, show that erythrocytes are also influenced upon by habitual smoking. In this context, it was our interest that no tendency of polycythemia was observed in the nonsmokers among the group W (group W-NS), whereas such tendency was most clearly remarkable in the group W-S. MCV as well as MCH levels were seen raised significantly in both smoker groups, W-S and S, compared with the levels of the control group. This means that in smokers, both hemoglobin content and packed cell volume are likely to increase more than erythrocyte count does. The relative distributions of MCV and MCH are shown in Fig. 5 and 6 respectively.

The smoker groups were further devided according to the number of cigarettes smoked daily to see if cigarette consumption was related to hematological finding. Table 4 tabulates the blood measurements in each subgroup. The numerical difference of each measurement between the subgroups was not so big as that between the control group and each subgroup, and little correlation became evident between cigarette consumption and the blood measurements as shown in Table 5. However, the ratio of increase in each blood measurement of the subgroups to the control group showed a fair consistency with the number of cigarettes smoked daily, as illustrated in Fig. 7.

Lastly, we examined statistically whether or not aging could have some influence upon smokers' blood measurements. Fig. 8 illustrates the mean values of blood measurements by age category in the group S and the control group. The means of leucocyte counts by age category in both groups are listed in Table 6. As shown in Table 7, we observed a rough tendency of smaller leucocyte counts in older age brackets in the smokers, whereas no such tendency was found in the control group. In order to conclude more confidently that aging can have an influence upon smokers' blood, further statistical study would be required using much bigger number of subjects.

Table 3. Differential Leucocyte Counts

	randomly selected				smokers WBC > 10^4/mm³	
	non-smokers		smokers			
number	77		88		210	
/mm³	$\bar{x} \pm \sigma$	median	$\bar{x} \pm \sigma$	median	$\bar{x} \pm \sigma$	median
stab.	212 ± 218.9	260	273 ± 219.1	303	481 ± 356.8**	525
seg.	3159 ± 1044.5	3280	3823 ± 1121.5**	4122	6598 ± 1778.1**	6600
baso.	55 ± 69.2	114	60 ± 79.0	92	77 ± 96.9	96
eosino.	196 ± 171.9	252	193 ± 174.3	267	262 ± 257.4*	324
lympho.	2628 ± 901.8	2689	2749 ± 865.5	2833	3972 ± 1187.7**	4055
mono.	103 ± 111.9	168	105 ± 119.2	167	154 ± 166.0*	245

* $P < 0.05$, ** $P < 0.01$
(t-test compaired with non-smokers)

Table 4. Blood Measurements by the Number of Cigarettes Smoked Daily

	non-smokers	smokers			smokers WBC > 10^4/mm³		
	0	~ 20	21 ~ 40	41 ~	~ 20	21 ~ 40	41 ~
number	179	103	79	11	128	172	37
WBC x 10^2/mm³	61.7±12.92	69.5±14.78**	73.5±16.62**	65.8±20.13	113.9±12.94	116.1±15.16	115.5±12.95
RBC x 10^4/mm³	493.3±33.30	494.2±30.69	490.5±35.40	482.0±34.64	501.9±40.52*	506.9±36.38**	505.4±34.39*
Hb. g/dl	15.1± 1.16	15.5± 1.02**	15.7± 1.17**	15.6± 1.20	15.6± 1.31**	15.9± 1.00**	16.0± 1.31**
Ht. %	44.5± 2.96	45.4± 2.69**	46.1± 3.29**	45.2± 3.48	46.1± 3.64**	46.9± 2.85**	47.0± 3.40**
MCH μμg	30.5± 1.93	31.4± 1.38**	32.0± 1.48**	32.3± 1.48**	31.1± 1.45**	31.4± 1.16**	31.6± 1.28**
MCV c-μ	90.5± 4.53	92.0± 3.84**	94.0± 4.21**	94.1± 5.02*	91.7± 3.75*	92.4± 3.27**	92.9± 3.01**
MCHC %	33.8± 1.08	34.2± 0.94*	34.0± 0.76	34.4± 0.77	33.8± 0.76	33.9± 0.68	33.9± 0.69
number	77	45	39	4	74	115	21
Stab. %	3.4± 3.11	4.4± 3.18	3.3± 2.97	4.8± 2.86	4.6± 3.54*	3.8± 2.51	4.3± 3.89
Seg. %	49.2±10.11	51.7±10.32	54.5± 8.26**	47.8± 5.76	56.7±10.17**	57.0±11.21**	55.9± 9.15**
Baso. %	0.9± 1.14	0.7± 0.99	1.0± 1.09	0.3± 0.43	0.6± 0.88	0.8± 0.87	0.4± 0.85
Eosino. %	3.1± 2.64	2.8± 2.49	2.7± 2.42	1.0± 0.71	2.1± 1.87*	2.3± 2.43*	2.9± 2.98
Lympho. %	41.6±10.76	39.0± 9.97	36.9± 7.68*	43.5± 4.15	34.5± 9.97**	34.8±10.56**	34.8± 8.09**
Mono. %	1.7± 1.83	1.4± 1.47	1.5± 1.52	1.3± 1.09	1.3± 1.36	1.3± 1.52	1.5± 1.30
number	168	96	78	10	85	117	23
ESR 1°mm	4.8± 4.99	5.0± 6.64	4.3± 3.99	3.8± 2.75	3.9± 3.88	4.3± 3.12	3.9± 6.20
ESR 2°mm	12.5± 9.68	11.6±11.39	110 ± 9.33	8.6± 5.12	10.8± 9.08	11.2± 7.24	9.2±12.74

* $P < 0.05$, ** $P < 0.01$
(t-test compaired with non-smokers group)

Table 5. Significance in the Difference of Blood Measurements by the Number of Cigarettes smoked Daily (t-test)

	smokers •	smokers WBC > 10^4/mm^3		
	~ 20 V.S 21 ~ 40	~ 20 V.S 21 ~ 40	21 ~ 40 V.S 41 ~	~ 20 V.S 41 ~
WBC	1.705	1.317	0.221	0.655
RBC	0.750	1.117	0.212	0.472
Hb.	1.223	2.242*	0.990	1.617
Ht.	1.570	0.166	0.185	1.328
MCH	2.802*	1.983*	0.923	1.873
MCV	3.322**	1.716	0.845	1.766
MCHC	1.535	1.194	0.288	0.711
Stab.	1.611	1.805	0.747	0.329
Seg.	1.343	0.185	0.415	0.318
Baso.	1.306	1.526	1.980*	0.961
Eosino.	0.184	0.299	0.982	1.286
Lympho.	1.459	0.194	0.029	0.124
Mono.	1.303	0.041	0.554	0.588
ESR1°	0.814	0.808	0.455	0.055
ESR2°	0.248	0.346	1.028	0.671

* $P < 0.05$, ** $P < 0.01$

• smokers consuming more than two packs of cigarettes daily are discarded because of small population.

Table 6. Leucocyte Counts by Age Bracket in Non-smokers & Smokers

age	non-smokers		smokers	
	N	$\bar{x} \pm \sigma$	N	$\bar{x} \pm \sigma$
		x 10^2/mm^3		x 10^2/mm^3
~ 29	47	62.6 ± 12.38	44	77.2 ± 17.66
30 ~ 39	63	62.9 ± 12.11	63	68.5 ± 17.02
40 ~ 49	40	59.6 ± 13.84	41	70.8 ± 13.70
50 ~	29	60.6 ± 13.74	45	68.3 ± 13.13
total	179	61.7 ± 12.92	193	70.9 ± 16.07

Table 7. Significance in the Difference of Leucocyte Counts between Non-smokers & Smokers (t-test)

		smokers			
		~ 29	30 ~ 39	40 ~ 49	50 ~
non-smokers	~ 29		2.536*	1.834	2.671**
	30 ~ 39	0.294		0.718	0.098
	40 ~ 49	1.055	1.260		0.854
	50 ~	0.646	0.800	0.293	

Fig. 1 Relative Distributions of Leucoyte Counts

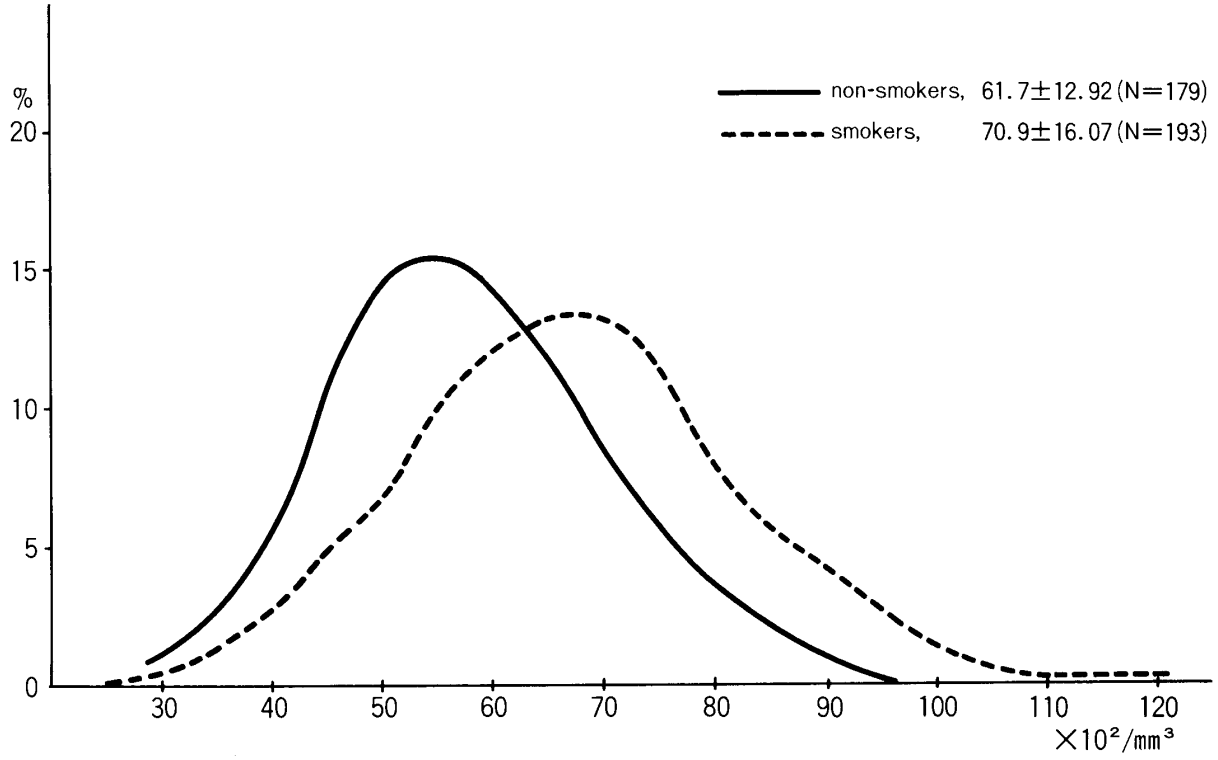


Fig. 2 Relative Distributions of Red Blood Cell Counts

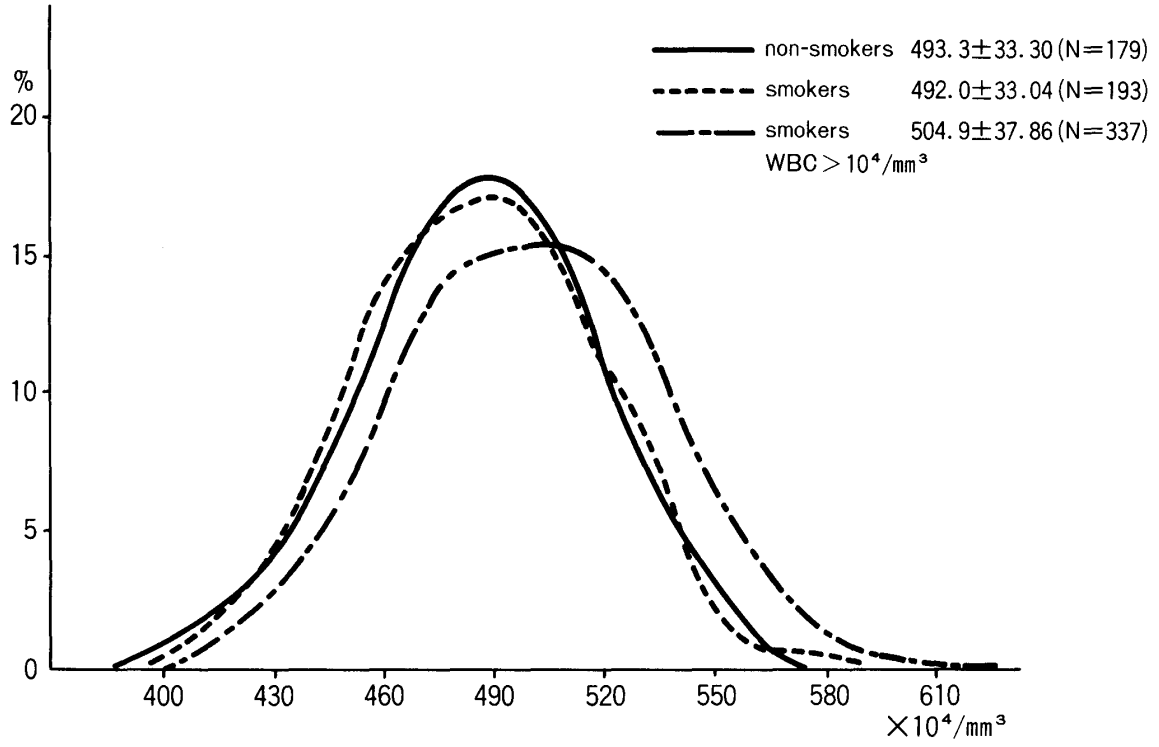


Fig. 3 Relative Distributions of Hemoglobin Content

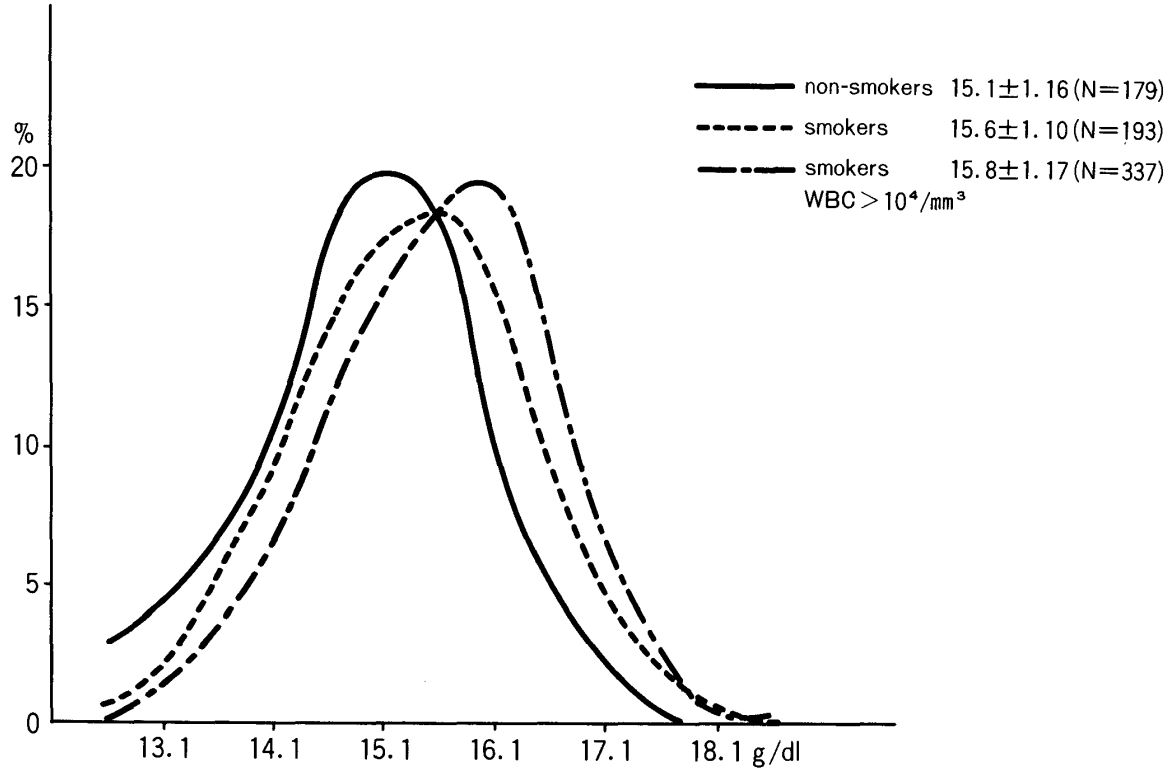


Fig. 4 Relative Distributions of Packed Cell Volume

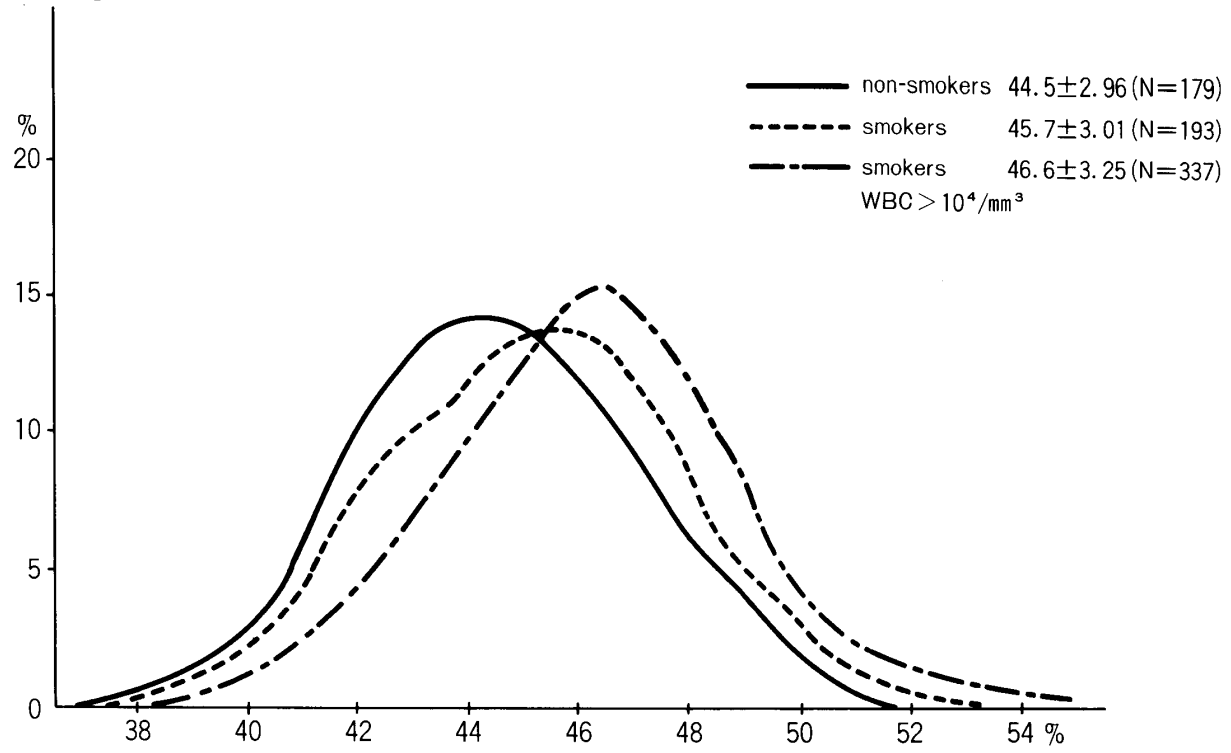
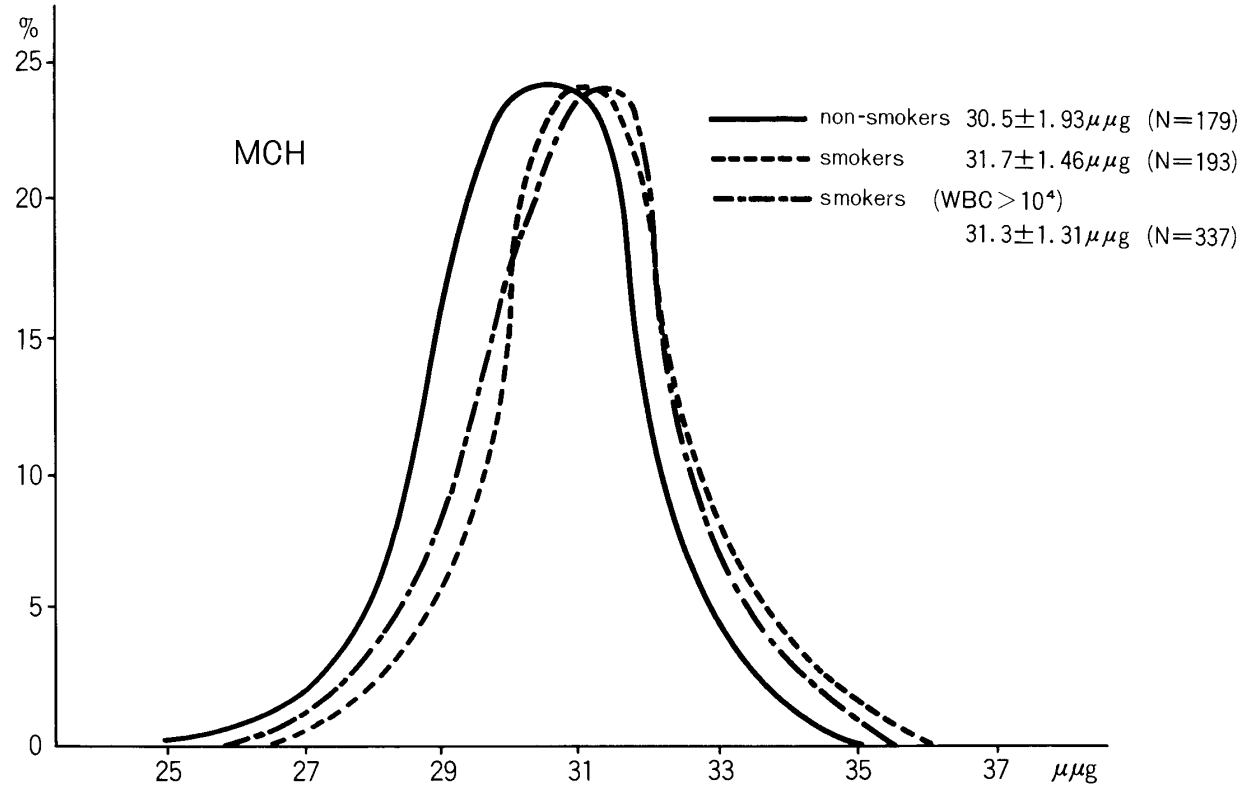


Fig. 5,6 Relative Distributions of MCH & MCV



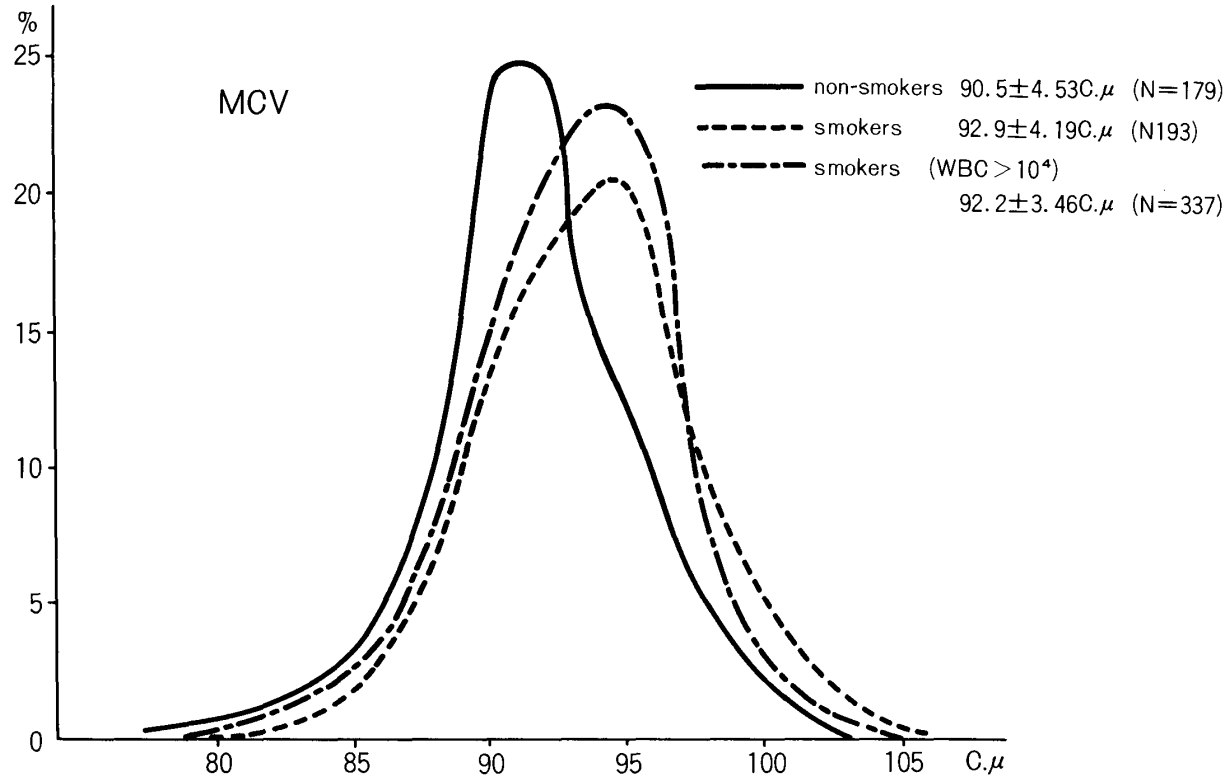


Fig. 7 Relation between Hematological Measurements and Number of Cigarettes Smoked Daily

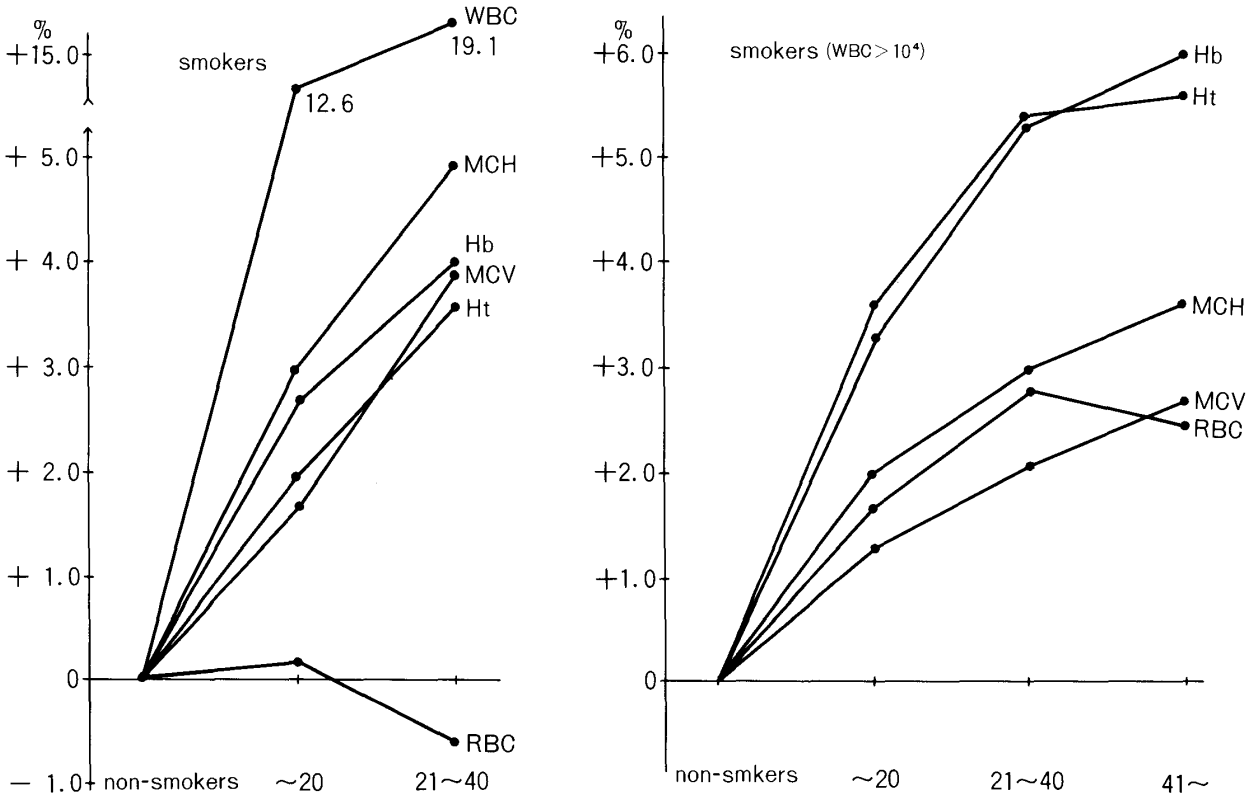
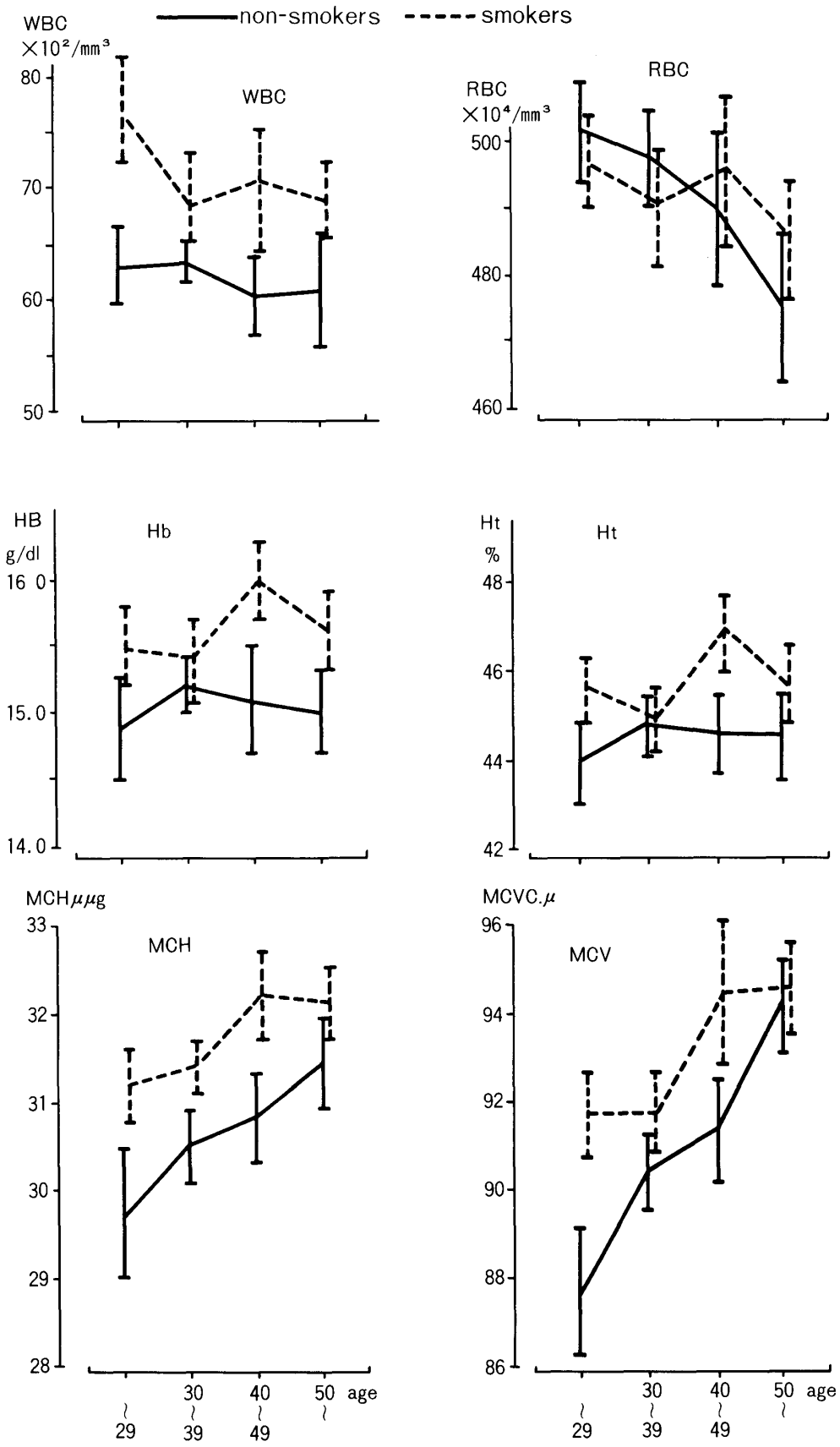


Fig. 8 Mean Values & 95% Confidence Intervals of Blood Measurements by Age Brackets



Discussion

Leucocyte count would be one of the commonest among the routine medical tests. But as it may show a wide range of fluctuation, influenced by a variety of such physiological factors as diet, exercise and stress, a certain discretion should be required when it comes to its appraisal. The unparalleledly wide deviation of leucocyte counts in physiological circumstances[2], in fact, would have been the main obstacle for doctors to evaluate the influence of smoking upon leucocytes.

A few reports, however, have so far been available with regard to leucocytes and smoking. As far as we know, Sheer[4] was the first to make an experiment on the matter as far back as in 1940. He noticed in his study that smoking made leucocyte counts increase temporarily in 50 examinees. The first epidemiological study was perhaps made by Howell.[5] He reported that the mean leucotyte count in 606 male nonsmokers was 5,950 ± 1,660/mm^3, and in 827 male smokers who smoked less than a pack of cigarettes daily and in 424 male smokers who consumed more than a pack, the means were 7,097 ± 2,010/mm^3 and 7,568 ± 2,312/mm^3 respectively. He wrote in his report that the difference of the leucocyte counts between the nonsmokers and the smokers was "impressive".

In the following year, Corre et al[6] made a survey on 4,264 men and reported that the mean leucocyte count of the smokers who inhaled cigarette smoke was 23.5% bigger than that of the non-smokers, though in the smokers who did not inhale, the elevation of the leucocyte counts was less striking. In our study, the average increase of leucocyte counts in the smokers was 14.9%.

It was 12.6% in the less-than-one-pack-a-day smokers and 19.1% in the heavier smokers. The figures are a little smaller than those reported by Howell and Corre, but if we had distinguised the subjects who inhaled and those who did not, the difference would have been more remarkable.

In 1973, Friedman et al[7] made an extensive field survey on smoking habits and leucocyte counts and stated that cigarette-induced leucocytosis was ubiquitous in both sexes throughout all ages in all human races. The fact was later confirmed by Fish et al[8] in 1975.

What in cigarettes makes the leucocytes increase, then? No persuasive answer would be so easily provided as for cigarette-induced polycythemia. We found that, although the increase of segmented neutrophils was the most contributory factor to leucocytosis, other types of leucocytes also showed increases in number to some extent. But the same finding was also observed in the nonsmokers with leucocytosis. None of the 559 smokers showed any sign of inflammation either in the physical examinations or in the laboratory data, except 2 CRP-positive cases who were otherwise healthy. Accordingly, a certain inflammatory process which might be taking place in the smokers' respiratory systems would not be considered the main cause of leucocytosis.

Another possible cause of leucocytosis in smokers would be the concentration of circulatory blood. There were found a significant correlations between leucocyte counts and erythrocytic measurements in the smokers as well as in the nonsmokers. But the mean leucocyte count of the smokers was more than 10% bigger than that of the control group, whereas the rates of increase in the erythrocytic measurements were comparatively low in the smokers. It was 3.3% in the case of hemoglobin content, which showed the biggest increase rate among the erythrocytic measurements. The difference would be inconsistently too big to attribute cigarette-induced leucocytosis to hemoconcentration.

Next comes a possible effect of nicotine and/or other chemicals in cigarettes. In fact, Friedman[7] suggested that nicotine might accelerate the secretion of catecholamine, which eventually made leucocytes increase. Kershbaum et al[9], on the other hand, inferred that cigarettes would raise the

concentration of 11-hydroxy-corticosteroid in blood and this hormone would bring about leucocytosis, featured by neutrocytosis and eosinopenia. In our study, however, we found that eosinophils rather increased, though less explicitly than neutrophils did. Corre et al[6] reported that leucocyte types were not influenced by smoking. Therefore, adrenal or hormonal commitment has not so far been persuasive enough to be approved in general.

The mechanism of cigarette-induced leucocytosis has, after all, yet to be made clear and its pathological significance has not been thoroughly evaluated. We think, however, that not only clinicians put also physicians in charge of industrial hygene and public health services should have the knowledge of the fact, lest they should be misled to incorrect conclusions in their diagnostics.

Furthermore, as the leucocytosis induced by smoking is undoubtedly remarkable, we think it necessary to recheck and establish the true physiological leucocyte count in consideration of smoking.

This manuscript was presented for the section "Health effects of physical environmental factors" at the XX International Congress on Occupational Health in September, 1981 at Cairo.

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