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TOXIC EFFECTS IN WOMEN EXPOSED TO INDUSTRIAL RUBBER SOLUTIONS

BY

J. L. HAMILTON-PATERSON, M.D.

Pathologist at Redhill County Hospital, Edgware

AND

ETHEL BROWNING, M.D.

H.M. Medical Inspector of Factories

This paper is the result of two years' investigation of the effects of industrial rubber solutions on the workers using them. Nowadays these are almost exclusively women. The solutions contain varying amounts of benzene and of the aromatic hydrocarbons benzene, xylene, and toluene; xylene and toluene are less toxic than benzene, but the latter is still used because of the difficulty of obtaining the former in sufficient amounts. Factory conditions have been much improved in recent years, and fatal cases of benzene poisoning are fortunately extremely rare; but even mild benzene intoxication may lead to irreversible changes in the haemopoietic bone marrow; also some people seem particularly susceptible, and develop signs of poisoning with only a limited exposure, particularly pregnant women (Meda, 1922; Hamilton, 1925; Smith, 1928; Hamilton-Paterson, 1941). It was hoped that as the result of this investigation it would be possible to identify early cases, of benzene absorption and remove them from contact before any permanent changes ensued. That this is possible will be clearly shown, and also that, with suitable periods of "rest," no harm will accrue to those who continue to work under these conditions.

Rubber solutions are used for a variety of purposes in industry, but this investigation was confined to their employment in a special manufacturing process in the aircraft industry. The examinations were carried out in 13 factories scattered over the country. The investigation has been conducted in two parts. In the first, sample groups in each factory, totalling 200 women, were clinically examined and had blood counts made. These counts have been compared with the counts of 200 control women. In the second part of the investigation all the women working in one factory have been similarly compared with a group of women in the same factory who had never been in contact with rubber solution. The effects of "rest" were also studied in this group of women. The manufacturing process in question involves the use of rubber solution and adhesive "cements" which contain aromatic hydrocarbons varying in strength from 5 to 20%: in practically all some proportion of this is benzene. Even though adequate ventilation is provided, as required under the India-rubber Regulations, 1922 (S.R. & O. No. 329), it is almost impossible for a woman, working in certain positions with a brush and an open pot of solution, not to inhale the fumes. In this way she is probably exposed to a concentration of benzene nearly as high as that in the solution itself. The practice in some workshops, under intensive production, of allowing large numbers of treated articles to remain in the workroom until perfectly dry may result in a further increase of the general atmospheric content of benzene. It should be remembered in this connexion that the general atmospheric concentration of benzene is by no means an entirely reliable criterion of benzene exposure, since individual workers may at any time be exposed to localized "pockets" of high concentration, particularly when working over open containers.

Clinical Results

A routine clinical examination, including condition of teeth, throat, lungs, heart, skin, and in many cases blood-pressure readings, was

carried out, and a careful case history taken. The chief points to which attention was paid in the case history were:

1. *Previous Occupation.*—A history of previous exposure to any toxic substance would naturally have to be taken into account in evaluating any disturbance of health or deviation from the normal blood picture. Since many of these women were in the 35-45 age group the previous occupation of a large proportion (about 40%) had been domestic. Among the other occupations represented were clerks, telephonists, waitresses, shop assistants, hair-dressers, dressmakers, mill-hands, weavers, and machinists. Only in two cases was there a history of occupation which possibly involved exposure to toxic solvents—one a rubber worker, the other a cleaner of aeroplanes. In both, the blood picture was within normal limits and there were no complaints of ill-health.

2. *Previous Illness.*—No history of previous illness likely to produce haematological disturbance was obtained except "long-standing anaemia" in one case, with a blood picture of mild microcytic hypochromic anaemia only. In 84% of all cases, in fact, no history of illness other than "childish diseases" was elicited; the remaining 16% gave a history of bronchitis (7 cases), tonsillitis (4), appendicitis (3), pneumonia (2), jaundice (1), rheumatic fever (3), heart trouble (2), gastric ulcer (1), gastritis (1), asthma (1).

3. *Symptoms.*—In all, 72 of the 176 women examined (approximately 41%) complained of symptoms probably referable to their occupation. These were in most cases not severe, and were in the following order of frequency:

(a) Lassitude (35).—Many of the women emphasized the fact that their fatigue, especially at night, had been particularly noticeable "since being on this job." It is possible, of course, that this symptom—particularly in women previously engaged in domestic work only, and now doing 47 to 55 hours a week in the factory, with some domestic duties in addition—may be attributed to excessive exertion rather than to benzene absorption; but many of the women appeared to relate their fatigue definitely to their occupation.

(b) Headache (27).

(c) Dizziness (25).—In one factory this symptom took an acute form, 18 women being overcome in one day by what they described as "fainting attacks" and "feeling drunk." Investigation showed that these attacks were very similar to the "benzene intoxication" reported by Kobert (1906) and others, and that the solutions used did in fact contain a high proportion of benzene. A combination of heavy fog, poor ventilation, and intensive production on the day on which this incident occurred was probably responsible for a sudden increase of the benzene content of the air of the workshop.

(d) Nausea (15).—The nausea and vomiting are probably not due to benzene but to other fumes evolved during the process. They seemed to be most pronounced in the mornings, particularly Monday mornings, when the shops had been closed over the week-end, and the fumes from the drying treated articles had accumulated.

(e) Vomiting (4). (f) Dyspnoea (6). (g) Loss of weight (3). (h) Gastric pain (2). (i) Bleeding from the gums not accounted for by local oral conditions (2).

An unusual complaint, for which no satisfactory explanation can at present be given, was that volunteered by several women that the faeces smelt strongly of the rubber solutions used.

4. *Menstrual Disturbance.*—Of these women 45 were between the ages of 40 and 55, and 7 of them complained of menorrhagia; this may probably be attributed to menopausal or pre-menopausal disturbance rather than to a benzene effect. Of the 131 younger women (aged 19 to 39) 4 complained of increased frequency of periods (which may have been associated with the change from domestic to factory life), and only one of recently increased loss. Five women were pregnant, but their health did not seem to be affected.

Haematological Results

The blood counts of the 200 women working with rubber solution have been analysed and compared with the counts of a group of 200 women, of similar age and conditions of life, who, so far as was known, had never been in contact with rubber solution. The results are shown in the accompanying Chart, in which frequency

Chart showing frequency distribution curves of red cells, white cells, polymorphs, and lymphocytes in the control group (x) and the group exposed to fumes of rubber solution (o—o).

distribution curves of the red cells, white cells, polymorphs, and lymphocytes are shown. It was impossible to treat the haemoglobin results in a similar manner, because the method of determining these varied with the conditions obtaining in the different localities where the investigation was pursued, and the methods employed did not all have the same degree of accuracy. This, with the possible variations in the standards used, introduces a degree of error which would render statistical analysis valueless. The differential counts were calculated on a basis of 200 cells where there was no deviation from the normal; 400 were counted in any doubtful case.

In the Chart the mean and its standard deviation for each set of observations are recorded, and from these the probable significance of the difference between means of the red cells, white cells, polymorphs, and lymphocytes of controls and rubber-solution workers can be calculated. If the difference between the means is greater than twice its standard error, then the difference is significant, and the chances are 19 to 1 against such frequency distribution curves being obtained from the same population of cells by random

sampling—i.e., if $\bar{X}_x - \bar{X}_o > 2 \sqrt{\frac{\sigma_x^2}{N_x} + \frac{\sigma_o^2}{N_o}}$ the difference is significant, where $\bar{X}_x$ and $\bar{X}_o$ are the means, σ_x and σ_o their standard deviations, and N_x and N_o the numbers of observations in the samples. The daily variations in the various elements of the blood count introduce a possible source of error into comparisons of this

kind, but so far as is possible this has been corrected by taking the counts at the same time of day. However, to allow for this and other errors arising from dilution and counting, we decided not to call a difference between means significant unless it was more than 5 times the standard error of the difference.

The results of these comparisons are shown in Table I, from which it will be seen that significant decreases in the mean values of the total white counts and the polymorphonuclear cells (a decrease in

TABLE I.—Comparison of Blood Counts of 200 Female Controls with those of 200 Females Working with Rubber Solution

	Controls		Rubber-solution Workers		$\sqrt{\frac{\sigma_x^2}{N_x} + \frac{\sigma_o^2}{N_o}}$	
	$\bar{X}_x$	x	$\bar{X}_o$	o		
R.B.C.	4.581	0.468	4.461	0.342	2.9	Not significant
W.B.C.	7.422	2.130	5.875	1.592	8+	Significant
Polys.	4.672	1.905	3.232	1.130	9+	
Lymphs.	2.277	0.842	2.375	0.721	1+	Not significant

polymorphonuclear leucocytes will hereafter be referred to as "neutropenia") are present in the women working with rubber solution. It will be seen that the standard deviation of the means is always larger in the control group, and this may be because the counts in this group were performed by several persons, whereas in the group being tested all the counts were done by one of us (E. B.). However, the final effect of this is to increase the value of the standard error of the difference between the means and thus decrease the ratio of the difference to the standard error; this will reduce the possibility of getting significant differences and not increase it. The monocytes, eosinophils, and basophils have not been included in this statistical comparison because their numbers are relatively small. Eosinophilia is, however, a recognized feature of the syndrome of severe chronic benzene poisoning.

In considering the individual cases of the test group the following scheme was followed in judging whether the woman should be considered as a possible case of benzene intoxication (Hamilton-Paterson, 1941). A plus sign was given for any of the following abnormalities: Hb below 20% Haldane or its equivalent, with either a macrocytosis or microcytic anaemia; white cells below 5,500 per c.mm.; polymorphs below 3,000 per c.mm.; eosinophils more than 160 per c.mm., with a white cell count less than 5,500 per c.mm.—suggestive symptoms. The presence of three plus signs is suggestive of benzene poisoning, and that of four or more plus values diagnostic in the absence of any obvious causation other than exposure to benzene.

Benzene absorption may of course be present with only one or two plus values, but true benzene poisoning in such a case is rare and is usually accompanied by well-marked clinical signs. The analysis showed that 34 women (17%) were possible cases of benzene poisoning, and that 19 women (9.5%) had four or more plus values and were probable cases; a total of 53 out of 200 (26.5%). The frequency with which the abnormalities occurred in these cases was: neutropenia 50 times, leucopenia 44 times, anaemia 41 times, suggestive symptoms 27 times, and eosinophilia 15 times.

In the second part of the investigation all the women in one factory working with rubber solutions were tested and compared with women in the same factory who had never been in contact with such solutions. In all, 92 subjects were tested—62 contacts and 30 controls. Blood counts on the contacts were done after six months' work with rubber solutions, and those who showed changes suggestive of severe benzene absorption were removed to another part of the factory, where they had no contact with the solutions. After such a "rest" period of three months they again had blood counts to see what improvement, if any, had occurred.

The results are shown in Table II. The numbers involved were too small to compare statistically; averages have therefore been taken and the maxima and minima in each group recorded. It will be seen that the results for the 30 control women agree quite well with the 200 controls in the first part of the investigation. Also, the averages for the 62 contacts are similar to those for the 200 contacts already recorded, except for the red cell count, which is higher than in the control group. The variations in the control and contact groups, as estimated by the maxima and minima, are of the same order. The results in this factory therefore agree well with those of the random samples from the larger number of factories, and, conversely, they suggest that the samples from the other factories closely represent the state of each factory as a whole.

Of the contacts 18 were removed and "rested" because of abnormalities of the blood counts. The averages of this group are shown in Table II, and also their averages at the end of the three-months rest period. The difference is striking: the white cell count has increased from 3,680 per c.mm. to 6,140 per c.mm., and the polymorphs from 1,750 per c.mm. to 3,410 per c.mm. The counts,

from showing a gross leucopenia and neutropenia, have returned to within normal limits. These results, indicating recovery from the depressive effect of benzene on the leucopoietic system, are closely comparable with those observed (e.g., Goodfellow, 1935) in radium and x-ray workers. To enhance the value of this observation three

TABLE II

30 female workers not in contact with rubber solution												
	Hb	R.B.C.	W.B.C.	P		L		M		E		B
				c.mm.	%	c.mm.	%	c.mm.	%	c.mm.	%	
Aver. . .	88.3	4.50	7,500	4,440	59.5	2,600	34.3	343	4.5	103	1.5	18
Max. . .	106	5.50	12,400	8,920		4,450		1,060		330		116
Min. . .	78	3.73	3,100	1,540		990		31		0		0
62 females after 6 months' work with rubber solution												
Aver. . .	90.7	4.71	5,400	3,100	56.25	1,900	36	290	5.45	102	2.1	4
Max. . .	112	5.64	10,700	6,950		4,620		1,000		448		62
Min. . .	78	3.75	3,100	1,120		750		48		0		0
18 females with blood change suggestive of marrow hypoplasia, after 6 months' work with rubber solution												
Aver. . .	86	4.54	3,680	1,750	47.7	1,630	44.2	202	5.5	73.5	2.1	18.5
Max. . .	104	5.92	4,800	2,740		2,310		360		192		40
Min. . .	64	3.73	3,000	1,120		1,180		48		0		0
The same 18 females after 3 months' rest away from rubber solution												
Aver. . .	86.3	4.61	6,140	3,410	55.5	2,360	38.4	276	4.5	92	1.5	6
Max. . .	100	5.49	8,100	5,750		3,900		576		300		132
Min. . .	74	3.86	4,000	1,580		1,340		100		0		0
3 females showing improvement of count with rest, and deterioration on further contact with rubber solution												
Case 1												
6/12 contact	88	4.16	4,200	1,680	40	2,310	55	168	4	42	1	0
3/12 rest	85	4.49	7,400	4,440	60	2,520	34	296	4	74	1	0
4/12 contact	88	4.4	4,100	1,480	36	2,540	62	492	12	0	0	0
Case 2												
6/12 contact	104	5.0	4,000	1,680	42	1,840	46	320	8	120	3	40
1/12 rest	90	4.47	3,800		38		48		11		3	0
4/12 rest	88	4.2	8,100	5,180	64	2,590	32	243	3	81	1	0
1/12 contact	86	4.3	5,500		40		52		4		4	0
4/12 contact	88	4.4	4,500	1,800	40	2,610	58	90	2	0	0	0
Case 3												
6/12 contact	90	4.81	4,400	2,640	60	1,450	33	308	7	0	0	0
2/12 rest	86	4.80	6,700	3,220	48	3,020	45	400	6	67	1	0
2/12 contact	82	3.92	4,100	2,050	50	1,600	39	370	9	82	2	0

of these women were put back on to the benzene process and again examined in two to four months' time. Their counts are shown in the lower part of Table II, and require but little comment. In each case further contact with rubber solution has led to deterioration of the count.

Urinary Sulphates

It has been suggested (Yant *et al.*, 1936) that the determination of the ratio of inorganic to organic sulphate in the urine would be useful in discovering early cases of benzene poisoning. Of the absorbed benzene 90% is excreted in the lungs (Feil, 1933). The remaining 10% is oxidized in the body, conjugated with sulphates in the liver, and excreted in the urine, thus lowering the inorganic/organic urinary sulphate ratio. The lowest normal ratio is about 80/20 (Schrenk *et al.*, 1936; Kammer *et al.*, 1938). Yant *et al.* (1936) state that a decrease in inorganic sulphate in the urine is a constant and early sign of benzene poisoning in animals. A distinct decrease occurred even with conditions of exposure which did not produce anaemia or leucopenia. They suggest that the striking nature and reliability of the change in animals exposed to benzene should serve as a measure of the exposure and potentially harmful conditions in workers, before injury to the organism has occurred. It is emphasized that the changes are merely indicative of exposure and not of poisoning or damage.

Seventeen women with neutropenia, in the factory which was completely surveyed, submitted specimens of urine. The sulphates

were estimated by the method of Peters and van Slyke (1932). All the results were within normal limits: the lowest ratio recorded was 81/19; all the rest were 85/15 or over. Twenty controls similarly examined gave readings ranging between 82/18 and 97/3.

These results would suggest that Yant's findings in animals cannot be applied to man, since in the series recorded here neutropenia certainly preceded urinary changes. In well-marked cases of chronic benzene poisoning the test is useful for confirming the diagnosis, as the inorganic sulphate may fall to below 50% of the total.

Discussion

As has been shown in the analysis of the results, the most striking changes in the blood counts are the leucopenia and the neutropenia. These are, of course, well known as the most common changes in the syndrome we call chronic benzene poisoning, before the development of the classical picture of aplastic anaemia, but it can be shown that they may occur in workers who show no clinical abnormality. Out of the 200 women exposed to rubber solutions and examined, 167 (83.5%) had white counts below the mean of 7,422 per c.mm. for the control group; 50.5% of the controls were below this mean. These figures are calculated from the frequency distribution curves (see Chart), and indicate that 33% of the test series have abnormally low white cell counts: 184 (92%) had lower polymorphs than the normal mean of 4,672 per c.mm., 55.5% of the controls being below the mean. Here 36.5% of the test series show an abnormally low polymorph count. In the analysis previously made 53 women (26.5%) of the test series were shown to be either suspicious or definite cases of severe benzene absorption; 44 of the series (22%) were suffering from leucopenia, and 50 (25%) had abnormally low polymorph counts. Thus it is clear that the white cell count has been lowered in 11% and the polymorph count in 11.5% of the test series where there was no indication of benzene poisoning.

It seems obvious, therefore, that there is a definite change in the white cell and polymorph counts before the appearance of other criteria which make a diagnosis of benzene absorption possible. The leucopenia and the low polymorph count run hand-in-hand—33% abnormality in the former and 36.5% in the latter; that is, the leucopenia is directly due to a reduction in the number of polymorphs. This is confirmed by the observation that there is no significant difference in the mean number of lymphocytes in either the test or the control group. The primary change is therefore the reduction in the number of polymorphs. This reduction is reflected in the bone marrow in a case reported by Piney and Hamilton-Paterson (1943) in which the myelogram showed a reduced percentage of myelocytes and metamyelocytes. To sum up, we may say that the essential change recorded in the test group of women is a neutropenia and that this makes its appearance before there is enough evidence to justify a diagnosis of benzene poisoning.

We have already shown that there is no significant difference between the means of the red cell counts of the exposed and control groups. On the other hand, 41 (20.5%) of the women picked out as possible cases of benzene poisoning showed anaemia—i.e., haemoglobin less than 80% and a colour index outside the limits of 0.85 to 1.10. The probable explanation of this anomaly is the different methods of haemoglobin estimation used—e.g., Haldane, Sahli, an alkaline haematin method (Clegg and King, 1942), and, on some occasions when no other was available, Tallqvist papers. It is possible that many of the results obtained by the last method were unreliable and may have caused us to mark a case as anaemic when in fact no such anaemia existed. It was because of this possible source of error that no attempt was made to compare the haemoglobin results statistically. In severe benzene poisoning, anaemia—either macrocytic and hyperchromic or microcytic and hypochromic—may develop, but the results of this investigation do not suggest that anaemia in any form is a constant early feature of the malady. Iron-deficiency anaemias may be difficult to distinguish from benzene anaemia because they may show a low white count with an abnormally low polymorph count; but administration of iron will probably separate them, because the few cases of benzene anaemia which we have been able to treat in this way have shown no improvement in the haemoglobin percentage and no reticulocytosis.

Eosinophilia has been stressed by some authors, particularly Dimmel (1932-3), as a feature of benzene intoxication. In the present series 18% of the exposed workers and 16% of the controls had more than 160 eosinophils per c.mm., while of the 53 affected workers 14 (26%) showed a similar change. Whitby and Britton (1942) give the normal maximum for eosinophils as 400 per c.mm. This may be so with a relatively high white count; with a white count of less than 5,500 per c.mm. 160 eosinophils should be regarded as the maximum.

Since this investigation has shown neutropenia to be the characteristic change found in early absorption of benzene, an examination of the incidence of neutropenia in the cases showing suspicious symptoms has been made. It may be stated at once that no such consistent relationship exists. Twenty-six (36%) of the 72 women presenting symptoms and 39 (37%) of the 104 symptom-free women had polymorphonuclear counts below 3,000 per c.mm.; that is, neutropenia occurs as often in women without symptoms as in those with them. Again, while three of the lowest polymorph counts recorded (1,600, 1,790, and 1,850 per c.mm.) occurred in three women complaining of more than one symptom—e.g., headache, dizziness, and nausea—even lower values (1,380 and 1,440 per c.mm.) were found in women with no apparent disturbance of health.

Menorrhagia has often been stated to be a leading symptom in chronic benzene poisoning. Eight cases occurred in this investigation, and seven of these were in women between the ages of 40 and 55. Is this menorrhagia due to benzene or to the menopause? As most of the cases occur between the ages of 40 and 55 it would appear at first sight as if the symptom was menopausal; it may be, however, that women at the menopause are more susceptible to benzene poisoning. Menorrhagia, in the absence of malignancy or endometrial abnormality, is a rare complication of the climacteric (Hamblen, 1939). We found 7 out of 43 women (16.2%) of the appropriate age group to be suffering from menorrhagia. This figure of incidence is higher than one would expect from a rare complication, but, as no attempt was made to exclude local disease of the uterus as a cause of the menorrhagia, it cannot be said definitely to be the result of increased susceptibility to benzene; it may, however, be suggestive. It should also be noted that the average polymorph count in these women (3,059 per c.mm.) is lower than in the younger women (3,603 per c.mm.).

There is no agreement in the literature about the subjective symptomatology of the climacteric. Norris (1919) states that 90% of healthy women experience no severe symptomatic disturbance; Hawkinson (1938), however, expressly states that 75% of all women suffer from distressing symptoms during this period. The personal factor is of course difficult to assess. Twenty-four of the 43 women examined (55.8%) complained of one or more of the following symptoms—lassitude, headache, giddiness, and menorrhagia—any of which may have been due to the climacteric or to the absorption of benzene. As this figure falls nicely between the two quoted, it cannot be said to indicate that benzene workers show more disturbance during the menopausal period.

The length of exposure to the fumes of rubber solution ought to be related directly to the neutropenia which has been shown to develop—that is, the longer the exposure the more marked should be the resulting fall in the polymorph count. An attempt was made to demonstrate this with the figures at our disposal, but it appeared that 59% of the women had been exposed for one year or less, and only 13% for a period between 2½ and 3 years. The average polymorph counts for these two groups were 3,163 per c.mm. and 3,445 per c.mm. respectively. As this last figure was calculated from only 26 women it is impossible to say that it presents a true picture of the whole population so employed. If, for argument's sake, it is assumed that the length of exposure does not increase the neutropenia, and therefore does not increase the risk to the worker, it would still have to be shown that the polymorphonuclear count returned to normal with rest after three years' exposure as well as after one year's exposure. Unfortunately all our figures for recovery were obtained on women with only six months' exposure, and at the moment none are available in respect of those with longer exposure.

The figures in the second part of the investigation, dealing with the changes in the blood counts after removal from

exposure to the solution, speak for themselves. After periods of rest up to three months the polymorph and white cell counts have risen and lie within normal limits. In the three women who were again exposed the counts very soon dropped. This observation, taken in conjunction with the previous observation that a lowering of the polymorph count is the earliest and most constant indication of benzene absorption, immediately suggests a method of controlling the absorption—particularly since, as already shown, there is no relation between symptoms and neutropenia. We would suggest that white cell counts should be done on all workers after an initial exposure of, say, six months: and that any who show neutropenia should be transferred to other work and recounts made after two months. If the count is then within normal limits the woman can be put back on her original work for a further period of six months and then be retested. If, however, there is no improvement in the count after the "rest" period the affected woman should be advised to give up work with benzene altogether, as it is possible that her bone marrow may be permanently depressed.

Conclusion

The toxic effects of the aromatic hydrocarbons (chiefly benzene) used in rubber solutions make the above precautions highly desirable. The substitution of a relatively non-toxic solvent such as solvent naphtha would render haematological control of the worker unnecessary; but so long as benzene is used it is advisable that the persons exposed should be given the protection of routine blood examinations. It may be noted that as the result of representations by the Factory Department the aromatic content of the rubber solutions used in this process has been limited to not more than 5% as one of the preventive measures required.

The question as to how the women with lowered polymorph counts react to infection is obviously important, and is one which we have not enough data as yet to answer. If the injury to the bone marrow is such that it does not recover with rest, it may be that infection will also be an insufficient stimulus to leucocytosis, and the patient thereby be deprived of an important defence mechanism.

The excretion of increased amounts of organic sulphates in the urine is a feature of severe benzene poisoning, but in this investigation no definite changes were found in people who clinically and haematologically showed definite early signs of the malady. It would seem, on the basis of this study, that benzene will produce haematological changes before it is excreted in significant amounts.

Summary

The clinical and haematological pictures of 200 women working with industrial rubber solutions are compared with 200 control women. Neutropenia is shown to be the commonest and earliest sign of benzene absorption.

It has been shown that there is no correlation between the symptoms complained of and the onset of haematological changes. This is important because clinical examinations alone are probably useless for the specific detection of early cases; but of course they have great value in the diagnosis of cases of deterioration in health due to other causes.

A possible method of preventing the onset of chronic benzene poisoning by regular white cell counts and suitable periods of "rest" is suggested.

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