

Preliminary Communications

CHROMOSOME ABERRATIONS
AND EXPOSURE TO AMBIENT BENZENE

We report here preliminary investigations of the possibility that men exposed to ambient benzene may show structural chromosome aberrations in lymphocytes cultured from the peripheral blood. The toxic action of benzene on erythropoiesis and myelopoiesis has been recognised since the early years of the present century. It is now becoming recognised that benzene is probably a leukæmogen and is especially liable to cause erythro-leukæmia.^{1,2}

SUBJECTS STUDIED

20 men were examined from a factory in which it had been found in 1962 that benzene was being used as a solvent. Since then toluene, free from benzene, has been used instead of benzene. These men are all considered to have been exposed to ambient benzene for periods varying from 1 to 20 years. The factory was visited on two occasions—in November, 1964, and in January, 1965. At the first visit blood samples were taken from 14 men selected because they had shown neutropenia in 1962. Study of cells from the blood-cultures provided prima-facie evidence for the presence of an unusual number of cells with chromosome aberrations. At the second visit blood samples were obtained from 6 additional exposed workers and also from 5 other men employed in situations in which exposure to benzene could not have occurred. The cells from cultures established at the second visit were counted and analysed without the cytologist knowing the source.

ASSESSMENT OF ABERRATIONS

Our approach to this problem has been identical to that for the study of radiation-induced aberrations. We scored the numbers of cells containing unstable aberrations (C_u cells) and of those with stable aberrations (C_s cells). C_u cells are those with dicentric, triscentric, or ring chromosomes, or with one or more acentric fragments, either alone or in association with these abnormal chromosomes. Such cells are considered unstable in that they are unlikely to survive more than two or three divisions, while there is no reason why rearrangements of chromosome material, producing recognisably abnormal monocentric chromosomes, should have an impaired capability of survival on division.

The numbers of C_u and C_s cells were compared with those in the cultures from the on-site controls and those from cultures established from males, randomly selected from the population, between the ages of 15 and 64 years. In all instances the cultures were harvested after between about 40 and 50 hours, inclusive of 3 hours with added colchicine. The necessity for standardising on early culture times has been discussed by Buckton and Pike.³

RESULTS

The findings in the exposed workers, the on-site controls, and the males from the general population are shown in table I. Those from the on-site controls and the randomly selected males do not differ significantly, and may be combined for comparison with the workers.

When the number of C_u cells in preparations from the workers are compared with those from the combined controls, the numbers in the workers are found to be

TABLE I—NUMBERS OF CELLS WITH CHROMOSOME ABERRATIONS

Group	No. of subjects	C_u cells		C_s cells		All C cells		Total cells
		No.	%	No.	%	No.	%	
Exposed workers	20	28	1.4	21	1.1	49	2.5	2000
On-site controls	5	3	0.6	2	0.4	5	1.0	500
Randomly selected males, 15-64 years	38	6	0.6	9	0.8	15	1.4	1060

For the exposed workers and on-site controls, 100 cells were counted and analysed per subject. For the randomly selected males 30 cells were counted and analysed in the majority, but in some fewer cells were studied.

significantly increased ($\chi^2=5.000, n=1, 0.05 > P > 0.02$). The difference is further emphasised by the complexity of the aberrations in the C_u cells (table II). This may be assessed by considering the number of chromosome breaks required to produce the observed aberration or aberrations, and expressed as the mean number of breaks per C_u cell. For the exposed workers the numbers of breaks varied from 1 to 6 (mean 1.68), while in the controls the mean number was 1.22, all but one cell requiring a single break.

The numbers of C_s cells in the exposed workers are greater than in the controls but not significantly so ($\chi^2=1.170, 0.30 > P > 0.20$). We have evidence from

TABLE II—ESTIMATED NUMBERS OF BREAKS REQUIRED TO PRODUCE OBSERVED ABERRATIONS IN C_u CELLS

Group	No. of C_u cells having had the following estimated number of breaks						Total breaks	Mean no. per C_u cell
	1	2	3	4	5	6		
Exposed workers	19	5	1	3	1	1	47	1.68
All controls	8	1	1	1	1	1	11	1.22

radiation studies that the numbers of these cells constitute a less sensitive indicator of a radiation effect. This is understandable, for by definition the great majority of C_u cells are microscopically recognisable; but there must be many stable chromosome rearrangements which cannot be detected in this way. The fact that a significant increase in C_s cells is not surprising in circumstances in which the yield of C_u cells, while significantly increased, is small.

DISCUSSION

Radiation exposure can produce comparable types of aberrations. We inquired, therefore, into the extent to which the exposed workers had been irradiated for medical purposes. None had had radiotherapeutic exposure; and the history of diagnostic exposure—mainly mass miniature radiography—is comparable to that for our controls. The most heavily exposed man had had several barium examinations of the gastrointestinal tract, and he showed only a single C_u cell containing an acentric fragment; this was probably without significance. We are confident that radiation exposure is not the explanation for the findings.

We are indebted to Dr. T. Lloyd-Davies, chief medical officer, and Dr. S. G. Rainsford, of Her Majesty's Factory Inspectorate, for their help and advice, and also to the medical officer and staff of the factory at which the studies were done.

ISHBEL M. TOUGH
B.Sc. St. And.

W. M. COURT BROWN
M.B., B.Sc. St. And., M.R.C.P.E., F.F.R.

Medical Research Council,
Clinical Effects of Radiation
Research Unit,
Western General Hospital,
Edinburgh

1. Downing, E. B. *Trans. Am. Industr. Med. Offrs.*, 1962, 11, 161.
2. Vigliani, E. C., Saita, G. *New Engl. J. Med.*, 1964, 271, 872.
3. Buckton, K. E., Pike, M. C. *Int. J. Rad. Biol.*, 1964, 6, 439.