RADIOBIOLOGY

Chromosomes of Two Cases of Human Chronic Myeloid Leukæmia

THREE reports have described an abnormally small chromosome (Ph^1) replacing one of the four smallest, acrocentric autosomes in the chromosome complement of cells from patients with chronic myeloid leukæmia[1–3]. The Ph^1 chromosome has been found in cultured peripheral blood or bone marrow cells from twenty patients with chronic myeloid leukæmia, ranging from untreated cases to those in terminal, acute stages, and a causal relationship between the chromosome abnormality and the disease has been suggested. Tough *et al.*[3] failed to find the Ph^1 chromosome in five cases of this leukæmia. Two of these had entered an acute leukæmia phase where diverse chromosome changes can be expected, whereas the other three cases had in common an unusually long history after diagnosis and followed a relatively benign course. Two of these latter cases had a previous history of radiotherapy for ankylosing spondylitis and there was a high probability that these leukæmias were radiation induced.

Two cases of leukæmia, which add to these findings, have been examined in this laboratory. The chromosome investigations were made on peripheral blood cells which had been cultured for two days by a modified form of the method of Moorhead *et al.*[4]. Case 1 is a 49-year-old woman who was recently diagnosed as chronic myeloid leukæmia, and was untreated at the time of the chromosome studies. The Ph^1 chromosome was found in 16 of the 27 cells which were examined (Table 1). This is a further example of the few cases which show that the presence of Ph^1 is not the result of any therapy measures causing chromosome breakage.

Table 1. CHROMOSOME COUNTS IN TWO CASES OF CHRONIC MYELOID LEUKÆMIA

Case no.	Chromosome counts 40 — 45	46	47	Total	Ph^1 present	Ph^1 absent	Ph^1 ?
1	1 1	24	1	27	16	10	1
2	– –	53	2	55	0	49	6

Case 2 is a 49-year-old man whose white cell count was first found to be high in 1956, and fluctuated afterwards with an overall tendency to increase. In 1959, sternal bone marrow cells showed a marked granulocytic hyperplasia with a particular increase in myelocytes and metamyelocytes consistent with a diagnosis of asymptomatic chronic myeloid leukæmia. An increased white cell count and splenic enlargement were successfully treated with 'Myleran' in 1960. This patient has a long varied medical history, and since 1944 has received a minimum of 33, and probably more diagnostic irradiations from which it has been estimated he has received a total skin dose of at least 180 r. Although the dose is small compared with those given in radiotherapy, the possibility that this leukæmia was radiation-induced cannot be dismissed. The Ph^1 chromosome was not found in any of the 55 cells, in which the small acrocentric chromosomes were studied (Table 1). This case appears to be of the same nature as the three cases described by Tough *et al.*[3], and supports their view of the existence of a distinct sub-group of chronic myeloid leukæmia characterized by unusually slow progression and absence of the Ph^1 chromosome.

The existence of such a group raises a problem as to the relationship of the Ph^1 chromosome to chronic myeloid leukæmia. If this leukæmia can occur without the Ph^1 abnormality, the latter can then be only one of its causes and, indeed, a different, more fundamental cause common to all cases of chronic myeloid leukæmia might be suggested. Alternatively, the malignant nature of the clinically benign cases without the chromosome abnormality may be doubted; the blood abnormality in these may have the nature of a long-term leukæmoid reaction, or it may be a pre-malignant stage, malignancy being consequent on the occurrence of the Ph^1 chromosome abnormality. The greatest interest of this group of cases lies in the possibility that they represent an elementary stage in the ætiology of the disease and that progression from their present malignant, but benign, course awaits the development of the Ph^1 chromosome abnormality. The Ph^1 chromosome is not therefore a primary event causing the leukæmia, but is a secondary effect of the neoplastic condition which has some other cause. Secondary chromosome stem-lines, which are important in the progression of tumours, usually result from chromosome breakage and reunion, which occur in an essentially random manner, and consequently tumour stem-lines show marked individuality and are rarely if ever repeated. The Ph^1 chromosome is the only chromosome abnormality which has been found consistently in neoplastic tissue, and as such, it differs from known secondary chromosome changes. If it is a secondary effect, and the result of random chromosome breakage, its presence in all cases of chronic myeloid leukæmia would require a rigorous selection for this particular chromosome abnormality.

The specificity of the Ph^1 chromosome to a particular form of leukæmia is striking, whether it is primary and causal or a secondary development.

I thank Dr. J. B. Howie for hæmatological data and for the estimate of the number of diagnostic irradiations received by case 2, and Mr. H. D. Jamieson for the estimate of the total skin dose received.

P. H. FITZGERALD

British Empire Cancer Campaign,
Radiation Biology Research Group,
Wakari Hospital,
Dunedin, New Zealand.

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Biogenesis of Glucobrassicin, the *in vitro* Precursor of Ascorbigen

RECENT work by Gmelin and Virtanen[1], concerning the isolation and elucidation of the structure of glucobrassicin, and its reaction with ascorbic acid in the presence of myrosinase to give rise to ascorbigen, prompted us to investigate some biochemical interrelations of indole derivatives in *Brassica oleracea* L. by means of labelled (radioactive) compounds. The main question in this connexion was why, in our previous communication[2], we were not able to prove the presence of glucobrassicin in our material. According to Gmelin[3], our method of working up the plant material was not suitable for demonstrating the presence of glucobrassicin in it. The reaction of glucobrassicin with ascorbic acid in the presence of