same in the two groups, it could be that one homozygote in the healthy group, but up to four heterozygotes in the geriatric group, are wrong guesses. This would somewhat reduce the significance of the findings.

Discussion

A slight but significant sex difference in ABO blood-group frequencies was recognized in 1943 when Fisher and Fraser Roberts, in a very large series, found the proportion of group A in men to be higher than in women, and that more of the latter were group O. This is very apparent in the healthy group in this series of elderly people but not in the geriatric group.

Age stratification of ABO blood group frequencies has also been looked for extensively (Fraser Roberts, 1948) and not found, but the author stated that the evidence covered adequately only donor ages approximately 18–60 years.

Aird *et al.* (1953) reported that carcinoma of the stomach is more common among group A individuals, and the evidence has been stated to be overwhelming (Fraser Roberts, 1959). Manuila (1958), however, thinks that the evidence for or against this association is not conclusive. The difference in group A proportions reported by Aird *et al.* between the gastric carcinoma cases and the hospital controls for Newcastle was less than the difference between the geriatric and healthy group in this series. Unfortunately their cases were not subdivided for age, although in a later report (Aird *et al.*, 1954) group frequencies by sex were given for some of the patients with carcinoma of the stomach drawn from a number of hospitals (locality unspecified). The authors noted that their figures did not exclude the possibility that the whole of the excess of group A in cancer of the stomach occurs in men, but thought this unlikely. In this report also it was noted that the gastric ulcer cases, which were drawn from three regions—London, Manchester, and Newcastle—showed that in both sexes the patients of group A were older than the patients of group O.

It is of interest also that in a series of 119 cases of gastric carcinoma (Jennings *et al.*, 1956) an association between group A and carcinoma of the pyloric end of the stomach was found, but only in men. And, again, in a study of blood groups in diabetes mellitus McConnell *et al.* (1956) found an excess of group A in diabetic men but not women.

In the present series the division is a simple one. One group was made up of in-patients in hospital, at least temporarily bedridden; the other of elderly people healthy enough to be active and ambulant. The significant change in the ABO groups—an increased proportion of group A—is localized to the healthy elderly male group. The series is reported in the hope that further work may elucidate whether it is mainly a northern phenomenon, and perhaps associated with the higher incidence of carcinoma of the stomach in the north, or whether some other selection is resulting in group A being more frequent among elderly people, and giving the appearance of carcinoma of the stomach, a disease of the elderly, being more frequent in group A persons.

So far as the Rh genotype differences are concerned, the heterozygote D/d, as in haemolytic disease of the newborn, again appears to be at a disadvantage, although among the homozygotes D/D in the healthy group it is the proportion of the "mixed" R_1R_2 which was most raised.

Summary

The ABO groups and Rh genotypes are reported on 633 persons over 64 years of age. These are divided into in-patients in geriatric units covering a wide range of illnesses, and a healthy elderly group. Significant differences in ABO distribution, showing as an increased proportion of group A, occurred in the healthy elderly male group. A significant increase in the proportion of homozygotes D/D among the healthy group is reported, most apparent among the males.

It is hoped that this series will help towards planning future work.

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Preliminary Communications

A New Chromosome Abnormality in Chronic Granulocytic Leukaemia

The presence of an abnormally small acrocentric chromosome (Ph¹ chromosome) has been described as a constant feature in the leucocytes of a high proportion of patients with chronic granulocytic leukaemia (Nowell and Hungerford, 1960a, 1960b; Baikie *et al.*, 1960; Tough *et al.*, 1961). We have confirmed this finding in four consecutive cases of chronic granulocytic leukaemia. In addition we now report a new abnormality occurring in one of these four patients. The leucocytes of this individual show a replacement of two of the smallest acrocentrics by abnormal chromosomes, one of which corresponds to the Ph¹, whereas the other is a minute fragment. The two abnormal structures are present either singly or in combination in the majority of the cells which have been analysed.

CASE REPORT

The patient, a man aged 34, was first diagnosed in August, 1954, as suffering from chronic granulocytic leukaemia. He was treated with splenic x-irradiation, ³²P, and busulphan, the disease remaining in good remission until March, 1961, when it entered an acute phase. After the administration of 6-mercaptopurine and prednisone a further remission occurred. Whereas in March, 1961, the marrow contained a high proportion of blast cells, which were also present in the blood, both marrow and blood showed a practically normal composition in June, and this remission has continued to date.

Methods of Examination.—The marrow was examined three times. The first examination, in March, 1961, was at the height of the acute exacerbation, when sternal marrow was obtained one hour after the intravenous administration of 6 mg. of demecolone ("colcemid") as suggested by Bottura and Ferrari (1960). The other two examinations were made in June and July, 1961, without previous administration of demecolone. The marrow samples were in each instance placed direct into hypotonic sodium citrate and treated according to the method of Kinlough *et al.* (1961), except that the final films were not made by squashing but by air-drying.

Three cultures of the patient's blood were made by the method of Moorhead *et al.* (1960) during July and August, 1961. During this period the blood count was normal except for the presence of a few (2-5%) myelocytes.

Results

Marrow.—The three specimens were examined for chromosome number and abnormalities; the findings are shown in Table I. In all specimens the diploid mode was 46 chromosomes. The Ph¹ chromosome was easily identified, and its prevalence is indicated in Table I. There was a second, much smaller, chromosome, which replaced a second small acrocentric and is shown as "minute" in

TABLE I.—Results of Marrow Examinations

Date	Chromosome Number (Diploid Cells)					Chromosome Abnormality				Total Cells Counted
	<44	44	45	46	>46	Ph ¹	"Minute"	Ph ¹ + "Minute"	Normal	
March	3	2	7	38	0	16	9	15	10	50
June	3	2	5	40	0	8	9	9	24	50
July ..	1	3	4	29	0	4	8	5	20	37

Table I and pictured in Fig. 1. It can be seen that some cells contained the Ph¹, others the "minute," and others still both the abnormal chromosomes. A translocation between chromosome No. 2 and one of the 6-12 group was seen in some cells (Fig. 2). This was present in 9 of 25 and 7 of 15 cells which could be fully analysed in the March and June specimens respectively. All cells containing the translocation also contained the Ph¹, and some contained the "minute." Furthermore, the marrow samples showed increasing numbers of tetraploid or near tetraploid metaphase plates. There were 14, 23, and 33 tetraploids among 100 cells examined respectively in each of the March, June, and July specimens. The modal number was 92 in those plates in which precise counts could be made (Fig. 3).

FIG. 1.—Karyogram of cell from direct marrow preparation: 46 chromosomes. In the place of the last pair of autosomes there are one abnormal small acrocentric chromosome (Ph¹) and one smaller fragment (the "minute").

FIG. 2.—Karyogram of cell from direct marrow preparation: 46 chromosomes. One member of the second pair of chromosomes shows an abnormally long lower arm. This appears to have arisen from a translocation in which one of the 6-12 group of chromosomes (Denver classification) was also involved. This abnormally short chromosome has been placed to the right of the second row of chromosomes. The X and Y chromosomes are shown to the right of the bottom row. The Ph¹ chromosome is also present in the "22" position.

FIG. 3.—Polyploid (tetraploid) cell from direct marrow preparation showing two "minutes."

Blood.—The chromosome numbers are shown in Table II. Again the diploid mode was 46. Only three "minutes" were identified, and the Ph¹ chromosome was seen only once. Five of 150 cells examined were tetraploid or near tetraploid. A possible translocation was seen in three cells in the August culture but in neither of the other two. Chromosome breaks were seen in four figures.

TABLE II.—Results of Blood Cultures

Date of Culture	Chromosome Number (Diploid Cells)					Chromosome Abnormality				Total Cells Counted
	<44	44	45	46	>46	Ph ¹	"Minute"	Ph ¹ + "Minute"	Normal	
14/7/61	0	1	1	9	0	0	0	0	11	11
21/7/61	0	0	1	11	2	0	0	0	14	14
17/8/61	3	1	3	36*	6	1	3	0	49	53

* Also 4 polyploid cells.

DISCUSSION

The work of the Philadelphia and Edinburgh groups has made it clear that the Ph¹ chromosome is the only constant chromosome abnormality found in the leukaemias. Nowell and Hungerford (1960a, 1960b) found it in seven and Tough *et al.* (1961) in 13 out of 18 patients with chronic granulocytic leukaemia. The abnormality is the result of loss of chromatin material from one of the smallest acrocentric chromosomes (No.

21 or 22 in the Denver classification), but no direct evidence has been put forward to show the mechanism responsible for the loss. It could be either a deletion or a translocation, with the distinction uncertain because the Ph¹ is only slightly smaller than the normal small acrocentrics, so that collateral evidence of translocation would be difficult to collect. It has been suggested (Ohno *et al.*, 1961) that the involvement of the acrocentric chromosomes in nucleolar organization may expose them to risk of damage. A fundamental and so far unsolved question concerns the relation of the Ph¹ chromosome to the leukaemic process; does its presence precede and possibly stimulate the onset of the disease, or is it a result of the leukaemic transformation? It is unlikely to result from treatment, since it has been found in untreated patients.

In our material there were two abnormal small acrocentric chromosomes, the Ph¹ and the "minute." These were present in a high proportion of cells in all three marrow specimens, during both the acute exacerbation and the subsequent remission of the disease. There were also a good many apparently normal mitoses, which was to be expected in a tissue with a mixed cell population like the marrow. Both abnormalities appeared to characterize fundamentally altered—that is, leukaemic—cells; and, since the composition of the marrow specimens was very different in the first specimen compared with the second and third specimens, it appears that the Ph¹ and the "minute" acrocentrics were contained in leukaemic blasts as well as myelocytes which could not otherwise be distinguished from their normal counterparts.

The new abnormality was interesting because of the extremely small size of the chromosome. If this had arisen from a translocation, one would have expected to find a reciprocal abnormality in another chromosome. In over 50 completely analysed figures we have not seen any suggestion of this. At the same time, the "minute" was itself capable of further division; many of the tetraploid figures contained two "minutes" (Fig. 3). We suggest that this chromosome abnormality arose from a deletion of chromatin material either before or after the onset of leukaemia. The same may well be true of the Ph¹ chromosome, and both might be the consequence of damage during nucleolar organization, as suggested by Ohno *et al.* (1961).

The rather constant translocation between the No. 2 and one of the 6–12 chromosomes was probably the result of treatment, either radiotherapy or chemotherapy. It occurred only in cells carrying the Ph¹, and its high frequency suggests that it must have conferred some selective advantage on the cells carrying it. The increasing proportion of tetraploid mitoses was of interest in view of the fact that polyploidy has been found associated with radio-resistance in some other pathological materials (De, 1961).

The three blood cultures showed, in strong contrast to the direct (non-cultured) marrow preparations, a notable paucity of all types of chromosomal abnormality. This suggests that the dividing cells in the blood were mostly non-leukaemic. The blood picture was practically normal on all occasions, and it is probable that most of the mitoses arose from large lymphocytes or monocytes which, in normal blood, are the only cells capable of division (Bond *et al.*, 1958). In the type of case here described the direct marrow preparations had thus a notable advantage over those derived from blood cultures, in that they yielded a far higher proportion

of the characteristic abnormal mitoses. This finding is in line with the arguments put forward by Sandberg *et al.* (1960, 1961). It also disposes of the contention that the Ph¹ chromosome may be an artifact produced in culture (Trujillo *et al.*, 1961).

SUMMARY

Repeated examination of the bone-marrow of a patient with chronic granulocytic leukaemia showed the presence of the Ph¹ chromosome as well as that of a hitherto undescribed minute chromosome replacing a second small acrocentric and probably originating from a deletion of chromatin material. These abnormalities were more easily found in direct marrow preparations than in cultures of the peripheral blood. They were present during remission as well as during an acute exacerbation of the disease.

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Medical Memoranda

Intra-atrial Sarcoma

When Prichard (1951) reviewed tumours of the heart he found that secondary tumours were 20 to 40 times more common than primary tumours, the most frequent primary sites being breast, lung, and the lymphatic system. Myxomas constituted nearly 50% of the primary cardiac tumours, with sarcomas second. Whorton (1949) reviewed the primary malignant tumours of the heart, and collected and classified 100 sarcomas. Among these were 18 round-cell sarcomas, 18 spindle-cell sarcomas, 11 pleomorphic sarcomas, and 5 were classified as leiomyosarcomas. Isolated case reports have been published since then, so that the total number of reported cases of primary malignant tumours of the heart is now probably about 160.

Primary tumours of the major blood-vessels are of even greater rarity—Giaccai (1949), reviewing reported cases, found 26 (9 benign and 17 malignant). Some are similar to the present case.

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