a fine network of arteries situated immediately under the mucous membrane between it and the muscularis mucosae (Special Plate, Fig. 4). From this plexus very fine arteries pass up into the mucosa vertically from the horizontal mucosal plexus, and in Fig. 5, on the Special Plate, the mucosal plexus can be seen giving off numerous mucosal arteries. The mucosa has a very rich blood-supply, and it is true to say that the mucous membrane rests on a carpet of blood-vessels, as has been well shown by Brockis and Moffat (1958) in their "neoprene" latex injections of these plexuses.

An injection of the venous system shows that the veins follow an identical pathway and pattern to the arteries, forming similar plexuses. The veins drain from the capillary plexus which is in the mucosa itself as small mucosal veins to join the submucosal plexus.

No muscular branches are given off by either the long or short arteries, the circular muscle and the taeniae coli receiving their blood-supply from the submucosal plexus. A muscular plexus is formed from arteries arising from the submucosal "macromesh" on the mucosal surface of the circular muscle, and from this plexus smaller arteries are given off which pierce the muscle to form the intramuscular plexus. Special Plate, Fig. 6 shows the muscle coats of the colon after dissection of the mucous membrane and the submucosal plexus, from which it can be seen that the muscle has a poor vascular pattern made up of small arteries.

Marginal Artery in Operations

Injection experiments have been performed on operative specimens which demonstrate the importance of preserving the marginal artery up to the point at which the colon is divided in operative resection. If a ligature is placed around the marginal artery at the midpoint of an operative specimen of colon, and one end of the artery is injected with a radio-opaque material of comparable viscosity to blood and under pressure equal to that of the patient's blood-pressure, the vessels in the wall of the colon will fill up to the ligature, but there is very little filling beyond this point. From this it can be concluded that there is a poor collateral circulation between the vasa recti and brevia, and, despite the richness of the submucosal plexus, it is too narrow in calibre to allow the development of any extensive intramural collateral. This is in contrast to the intramural collateral that develops in the stomach and to a lesser extent in the small intestine. Care must, therefore, be taken not to ligate the marginal artery proximal to the proposed site of an anastomosis, and it is inadvisable to "clean" the "mesenteric" border of its vasa recti at the site of anastomosis or possibly to damage these vessels by removing the appendices epiploicae, as this would produce ischaemia at the ends of the gut which is being anastomosed.

Many post-operative fistulae occurring after anastomosis in the colon are in part due to the inadvertent devascularization of the ends of bowel following misplaced ligature of the marginal artery. It has been emphasized by Naunton Morgan (personal communication) that the marginal artery should be ligated 1 in. (2.5 cm.) beyond the site of section of the colon, thus obviating the danger of the marginal artery being distorted after mobilization of the colon. It is often difficult to verify the viability of the colon during resection procedures, in particular where high ligation of the inferior mesenteric artery has been performed in operations on the distal colon and rectum. Pulsations

of the larger vessels may be markedly diminished because of spasm from handling, and the colour of the large intestine is not always a safe guide; but the adequacy of the blood-supply is really proved by the division of the marginal artery below the selected site of resection, before the application of artery forceps.

Summary

The extramural and intramural vessels of the colon have been reinvestigated, using necropsy and operative specimens injected with "micro-opaque" solution, and a technique of microradiography has been developed to demonstrate the intramural plexuses. The importance of the marginal artery during operative procedures on the colon is emphasized.

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INCIDENCE OF SOME AETIOLOGICAL FACTORS IN HUMAN LEUKAEMIA

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Radiations, chemical agents, and heredity are among the factors suspected of being concerned in the cause of some cases of leukaemia. An investigation designed to estimate the incidence of these and other factors in an unselected population has been in progress for some time, and the preliminary results of the first two years are now reported. With the aid of a detailed questionnaire, interviews were conducted by doctors with as nearly as possible all new patients having leukaemia (including myelomatosis) throughout New Zealand, and with control patients matched for age and sex. The results were centrally coded and analysed. The controls were chosen from hospital patients. Since this might be thought to introduce bias, especially in measuring exposure to drugs and x rays, two further control groups were formed to test this possibility. These consisted

(1) of random ambulant patients seen in the surgeries of private doctors, and (2) of hospital patients matched for age and sex with the patients in the former group. The results in all three control series were identical, and the possibility of systematic bias in the controls appears to be excluded.

The questions asked in the interviews referred to personal details, medical, occupational, and family history, and exposure to physical and chemical agents. This report deals with the information obtained on the first 298 patients, who are estimated to represent about 80% of new leukaemia cases occurring in New Zealand in two years. Eventually nearly 90% of all cases in the country should become available for analysis.

Results

Radiation.—No difference between the groups was found in the incidence of diagnostic x-irradiation, as assessed either by the type and topographic distribution of the examinations or by the total skin doses received during the 10 years preceding the onset of the disease in question (Table I).

TABLE I.—Skin Doses Received Over 10 Years from Diagnostic X-irradiation*

Dose (r)	Percentage of Patients Receiving Dose				
	Acute	Chronic Granulocytic	Chronic Lymphocytic	Myeloma	Controls
0	47	41	24.5	30.5	41
1-5	39.5	44	59	48	44
6-10	8	8	10	16	8
11-20	4	6	4	3	6
21+	1.5	1	2.5	2.5	1
Total average annual dose per patient	260 mr				280 mr

* Excluding all examinations made for the diagnosis of the condition in question, and excluding dental x-ray examinations.

Skin doses were calculated from the figures of Webster and Merrill (1957) modified for New Zealand conditions. No difference was found in the incidence of diagnostic abdominal irradiation of mothers during the pregnancies leading to the birth of leukaemic children or their controls, but the figures (5 of 43 in leukaemics, 5 of 34 in controls) are, so far, too small for evaluation and do not conflict with those in the much larger series of Stewart *et al.* (1958). There were 21 leukaemic subjects and 8 controls who had had radiotherapy by means of x rays. Their doses are shown in Table II. The excess of high doses in the

TABLE II.—Doses from Therapeutic X-irradiation

Integral Dose* (mega-g r)	No. of Patients	No. of Controls	Weighted Marrow Doses† (r)	No. of Patients	No. of Controls
Less than 0.1	10	5	Up to 10	11	6
0.1-1.0	2	1			
1.1-1.5	0	2	11-100	2	2
1.6-10	5	0			
11-21.7	4	0	100-1,000	8	0

* Integral dose calculated from first approximation: I.D. = 1.4 × skin dose × field area × $\frac{1}{2}$ -value depth tissue.

† Weighted marrow dose: Depth doses weighted for distribution of active marrow in standard man (United Nations, 1958). Bone assumed to be equivalent to 1 mm. Al added to incident radiation.

leukaemia group was obviously significant (corrected χ^2 6.06; 0.02 > P > 0.01). No similar difference was found in the incidence of past radium treatment.

Chemical Agents and Drugs.—No difference was found between the groups.

Family History.—A possibly significant excess of first-degree relatives (parents, siblings, children) with cancer was found in patients with chronic lymphocytic but in no other form of leukaemia (36 relatives of 66 patients; 104 relatives of 296 controls. Corrected χ^2 3.75; P=0.05). The observed incidence among controls of 35% first-degree relatives with cancer corresponded to an expected figure* of 31%. There were 17 leukaemia patients with four first-

degree and 16 second- and third-degree relatives with leukaemia, and four controls with no first-degree and four second- and third-degree relatives with leukaemia. The significance of this excess is doubtful, as there was a deficit of expected relatives* among the control group. Multiple cases occurred in three families.

Mongolism.—Among the leukaemic children there were one mongol and one other feeble-minded individual.

Other Factors.—Among 12 Maori patients with leukaemia only one had the chronic lymphocytic form. Among a total of 42 Maori deaths from leukaemia (not in the main survey) registered over five years there was only one certain and one possible death from the chronic lymphocytic form, giving an incidence of 2.5-5%, compared with 25% in the general population. This type distribution resembles that in some other non-Caucasian races (Wells and Lau, 1960). The incidence of past and concurrent cancer was 1% in controls (expected figure, from national statistics, 0.8%) but 19.8% in chronic lymphocytic leukaemia, a very highly significant difference (corrected χ^2 27.713; P<0.01), even when allowance was made for the differing age distribution in the two groups.

Discussion

The incidence of recognized causal factors was low in this material. There were nine cases (all treated by radiotherapy) in which radiation may have helped to produce leukaemia. Mongolism is known to be sometimes related to acute leukaemia (Krivit and Good, 1957). Even if we add the doubtful familial cases, there are still only 21 instances (9 radiotherapy, 10 familial, 2 mongol or feeble-minded) out of 298 in which the disease could possibly be attributed to known "leukaemogens." This is a mere 7%, and it remains doubtful if further work on similar lines will add greatly to it. On the other hand, our findings make evident the special position of chronic lymphocytic leukaemia: a disease with a characteristic racial distribution, with a very high personal and a possibly raised familial incidence of cancer, and with known distinctive clinical features may well be chiefly determined by genetic factors. Whereas a continuing pursuit of "leukaemogens" does not therefore appear to be a promising way of clarifying the aetiology of leukaemia as a whole, the further investigation of genetic and other factors possibly concerned in its chronic lymphocytic variety may well lead to a clearer illumination of a limited field.

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$$* \text{Expected figures calculated from: } n = \frac{150 \times X}{Y} \quad \text{Where X is}$$

the number of known cases of the disease in New Zealand, Y the population of New Zealand, and 150 the known total age in years of the average New Zealand family.