FAILURE OF MASSIVE DOSES OF VITAMIN B₁₂ IN ACUTE LEUKAEMIA

BY

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This trial of vitamin B₁₂ in acute leukaemia was carried out at the suggestion of the Medical Research Council. Clinical workers had reported the apparent occurrence of remissions in patients with malignant disease who had been treated empirically with vitamin B₁₂. It was conceivable that vitamin B₁₂ might promote the differentiation of leukaemic cells into normal leucocytes, on the analogy of the restoration of normal blood formation in pernicious anaemia. Messrs. Glaxo Laboratories made available a supply of vitamin B₁₂ in ampoules containing 1 mg., which is approximately 1,000 times the maintenance dose in pernicious anaemia. The dosage decided on was 1 mg. intramuscularly a day, regardless of the type of the acute leukaemia or the age of the patient.

The co-operation of physicians and clinical pathologists in the Oxford region enabled us to treat and follow up 25 unselected cases of acute leukaemia in less than a year. Diagnosis was made on clinical and blood findings and confirmed by marrow aspiration. Marrow puncture was repeated in the few cases in which the peripheral blood showed much change. The cases were not divided into treated patients and untreated controls, because the usual course of acute leukaemia, including the frequency of partial and complete remissions, is now well known (Bierman *et al.*, 1950; Southam *et al.*, 1951), and any important modification as a result of treatment should soon become apparent. The prescription of blood transfusions and antibiotics was left to the discretion of the physician in charge of the patient, but other remedies such as x rays, radiomimetic drugs, A.C.T.H., and cortisone were not used.

The results are shown in the Table. The patients treated consisted of 11 females and 14 males, their ages varying between 3 and 69 years; 10 were 14 years of age or less, and the average age was 25 years. The cell types were as follows: 10 acute myeloblastic or myeloid, six undifferentiated cell type, five lymphoblastic, and four monocytic. The average time from onset of symptoms to diagnosis was

approximately seven weeks. The survival after diagnosis ranged from 156 days to 2 days, with an average of 52 days. The total duration of the disease thus averaged about 14½ weeks, and there were no instances of noticeably long survival.

All the patients are now dead. None showed a complete remission; the nearest was Case 2, who had a good clinical remission lasting three months, during which time his blast cells dropped from 20% to 5%, but the haemoglobin did not rise above 60% and the platelet count remained at 50,000 per c.mm.

No patient became afebrile on treatment, nor was there any substantial retrogression in the size of the spleen or glands. Only objective signs of clinical improvement, such as gain in weight or rise in haemoglobin, have been recorded. Six cases (Nos. 1, 2, 3, 7, 8, and 9) had a partial remission, and an additional 10 felt better but did not show any objective change in their condition. No toxic effect attributable to the B₁₂ was observed.

Summary

Twenty-five patients with acute leukaemia have been treated with massive doses of vitamin B₁₂. None lived for more than five months after beginning treatment. No complete remissions occurred, but six patients had partial remissions and a further 10 reported feeling better.

There is no evidence from this series to suggest that the prognosis or clinical course of acute leukaemia is altered by adding vitamin B₁₂ to other treatment.

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USE OF A.C.T.H. IN AGRANULOCYTOSIS

BY

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The papers by Discombe (1952) and by Dudley Hart *et al.* (1952) prompt me to publish the following notes. In the former article the relatively frequent occurrence of agranulocytosis on the Continent is compared with the rarity of the condition in this country, and is explained by the popularity which amidopyrine has gained and still maintains outside Great Britain. My own experience (Fuld, 1931) of having observed three fatal cases of agranulocytosis within six months in 1930 in a medium-sized German hospital where "pyramidon" (amidopyrine) was the standard drug, only second to aspirin in its frequency of administration, supports Dr. Discombe's conclusions. This is, however, only in retrospect, as I was quite unaware of the relationship of amidopyrine to agranulocytosis at that time.

In the past 19 years I have, of course, come across a number of patients with more or less severe leucopenic reactions following sulphonamides and thiouracil preparations, but no true case of agranulocytosis was met with until May, 1952.

Case Report

A woman aged 65 was referred by her doctor on May 30, 1952. She had had remarkably good health until a year previously, when she complained of lack of energy and

Results of Treatment

No.	Sex	Age in Years	Diagnosis	Duration of Symptoms Before Diagnosis	Survival After Diagnosis in Days	Total B ₁₂ in mg.	Partial Remission
1	F	4	Acute undifferentiated	8 weeks	156	68	+
2	M	40	Acute myeloblastic	2 "	130	130	+
3	F	4	" undifferentiated	10 "	120	48	+
4	F	17	Acute monocytic	12 "	103	103	0
5	M	69	" "	8 "	96	96	0
6	M	63	" myeloblastic	14 "	90	16	0
7	F	29	" monocytic	3 "	90	65	+
8	M	44	" lymphoblastic	2 "	70	70	+
9	M	3	" "	8 "	65	60	+
10	F	3	" stem cell	12 "	62	56	0
11	M	30	" monocytic	12 "	58	48	0
12	M	14	" myeloblastic	4 "	45	45	0
13	M	22	" undifferentiated	2 "	44	44	0
14	M	34	Acute lymphoblastic	4 "	40	40	0
15	M	56	" "	3 "	35	35	0
16	M	23	" myeloid	7 mths	21	21	0
17	F	19	" "	7 "	18	18	0
18	M	4	" "	3 weeks	11	11	0
19	F	43	" myeloblastic	9 "	8	8	0
20	F	54	" myeloid	5 "	8	8	0
21	F	47	" lymphoblastic	16 "	6	6	0
22	M	30	" myeloblastic	8 "	6	6	0
23	F	41	" erythraemic myelosis	3 "	5	5	0
24	M	14	Undifferentiated	4 "	5	5	0
25	F	34	" "	12 "	2	2	0