Continuous culture of neoplastic cells is a fairly standard technique in many microbiological laboratories. The majority of such lines are derived from tumours of animal and human origin and one of the advantages of this type of culture is that large numbers of cells are constantly available for various biochemical, biological and pharmacological experiments. While there are many continuous cultures derived from tumours, there are exceedingly few such cultures in existence derived from acute leukaemic cases in which the cell present is in fact neoplastic in its own right and capable of inducing tumour formation regularly on inoculation into animals.1 The CEM tumour cell line at the Childrens Cancer Research Foundation in Boston is the best documented. A number of other lines have been described. However, in these the cells are exceedingly slow growing and there is often the probability that the cells multiplying in the cultures have in fact been derived from non-neoplastic lymphocytes or monocytes present in the original inoculum.2 In the present study, attempts have been made to initiate continuous cultures from the peripheral blood cells of patients with acute myeloblastic leukaemia.

**MATERIALS AND METHODS**

The material comprised 20 patients satisfying the usual haematologic criteria for acute myeloblastic leukaemia. As large numbers of cells are needed to initiate cultures, only patients with peripheral leucocyte counts of 20,000 per cmm. or greater were selected. Patients were not receiving chemotherapy at the time the blood samples were drawn for culture.

A total of 34 cultures were set up from the 20 patients. Blood (20 - 40 ml) was withdrawn by venepuncture and anticoagulated with 20 units heparin per ml. The red cells were allowed to settle by gravity for 30 - 60 minutes at room temperature and the supernatant plasma was aspirated. The plasma was then lightly spun and the supernatant removed, and the cells were resuspended by making them up to 10 ml with Hanks BSS. They were then counted and 50 or 100 ml of media were then inoculated with sufficient of the cell concentrate to give culture concentrations of 2 - 3 x 10⁶ per ml. Culture media used were M 150 and MEM with 10% supplementation of bovine serum, foetal calf serum or autologous plasma. The majority of the cultures were set up in static phase, while a few spinner cultures were also initiated. Counts were carried out at varying intervals and viability was assessed by nigrosine exclusion. Old media were withdrawn and fresh added when cultures became too acid.

In many culture systems, optimum population density may be a significant factor in the viability of the cultures. When it became evident after some weeks that the cultures would not remain viable, periodic concentration was undertaken by repeated centrifugation and resuspension of the cells in a 50/50 mixture of old (conditioned) media and fresh media.

**RESULTS**

It became apparent after a few months that although cultures remained alive for many weeks—as shown by their ability to acidify the media—there was little, if any, tendency for the cells to multiply. As can be seen from Fig. 1, which is a composite representation of many cultures, the counts gradually decreased. The initial fall-off in cell count was exponential with a half-life of 28 days.

**DISCUSSION**

We have been unable to establish long-term continuous cultures of leukaemic myeloblasts by standard culture methods or by repeated concentration of cultures, using various serum supplements. These findings pose the perennial question which plagues workers in the leukaemic field—viz., is the leukaemic cell a particularly fastidious cell in its serum, amino acid and vitamin requirements? That this might be the case is borne out by certain findings with the CEM line in Boston. This shows exquisite sensitivity to minute increases in concentration of thymidine in the culture medium.3 In order to test such a hypothesis, enormous numbers of cultures from individual cases would have to be set up in order to cover the large number of permutations possible. Such undertakings are exceedingly vast and costly and probably not practicable except in isolated selected cases.

Or are we in fact, in leukaemia, dealing with cells which are not able to undergo unlimited mitoses and which
in fact have a life-span rather longer than their non-neoplastic counterparts? In other words, is the leukaemic cell an 'end cell' which cannot be induced to undergo mitosis unless certain profound immunological and cybernetic factors are present—factors which as yet are present in the milieu of the patients, but which cannot be channelled into the culture broth?

SUMMARY

Attempts have been made to establish continuous culture from the peripheral blood cells of 20 patients with acute myeloblastic leukaemia in relapse. Although cultures remained alive for many weeks there was little tendency for cells to multiply.

A COMPARISON OF ALPHA-METHYLDOPA (ALDOMET) AND ST155 (CATAPRES) IN THE TREATMENT OF HYPERTENSION*

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Physicians are persistently inundated with information introducing new hypotensive drugs and it is difficult to finish a critical assessment of any one drug before it is replaced or regarded as redundant. With this in mind it was thought desirable to compare Aldomet with Catapres in a selected group of patients whose attendance record at the hypertension clinic and reliability for taking therapy had previously been assessed. Thirty patients suffering from mild to moderate hypertension were initially put on Aldomet for a period of 6-8 months and the same group of patients was switched to Catapres for a similar period. It was decided to compare Aldomet with Catapres because their side-effects were alike and both drugs had previously been found useful in the treatment of mild to moderate hypertension. Our criteria in the selection of mild to moderate hypertension have been previously described and we have regarded patients with a resting diastolic blood pressure of between 140 and 160 mm.Hg or grade 3 retinopathy (presence of exudates and haemorrhages) as having moderate hypertension and those patients with a resting diastolic blood pressure of between 100 and 140 mm.Hg or a grade 1-2 retinopathy (presence of arterial changes and arteriovenous nipping) as having mild hypertension.

MATERIAL AND METHODS

Thirty patients (20 Indian and 10 Bantu) were selected for this trial. Twelve were male and 18 female. The basic types of hypertension and age distribution considered in this trial were as follows: (a) essential hypertension (24), (b) chronic pyelonephritis (2), (c) toxemia of pregnancy (3), and (d) malignant hypertension (1).

Eight patients were between 30 and 40 years of age, 14 patients were 40-50 years, and 8 patients were aged 50-60 years. The fundal changes were grade 0 in 13 patients, grade 1 in 5 patients, grade 2 in 10 patients and grades 3 and 4 in 1 patient each.

Three of the patients had had a previous cerebrovascular episode, 12 had evidence of renal involvement as detected by the presence of albuminuria, and 10 patients had electrocardiographic changes of left ventricular hypertrophy or chest X-ray findings of left ventricular enlargement.

The aim of treatment was to reduce the standing diastolic blood pressure to as near normal levels as possible without side-effects. A blood pressure which was maintained at 160/100 mm.Hg or less, supine or standing, was regarded as satisfactorily controlled.

RESPONSE TO THERAPY

The average dosage initially required to lower the blood pressure to a diastolic level of 100 mm.Hg or less was 456 mg. twice a day for Aldomet, and 180 μg. three times a day for Catapres.

The dosage of Aldomet varied from 250 mg. to 2 G twice a day. The average dose was 458 mg. at the same intervals. The dosage of Catapres varied from 75 to 750 μg. and the average dosage was 287 μg. three times a day.

There was no difference between Bantu and Indian patients in their response to therapy, and no rise in blood urea on either form of therapy. The period for albuminuria to disappear on Aldomet therapy was one week in 1 patient, one month in 7 patients and two months in 3 patients. One patient had persistent albuminuria. The period for albuminuria to disappear on Catapres was one week in 1 patient, one month in 2 patients and two months in 4 patients. Two patients had persistent albuminuria.

One patient on Aldomet therapy developed a cerebrovascular episode. This did not occur with Catapres therapy.

Side-Effects

The side-effects due to past therapy which did not recur with Aldomet were the following:

1. Impotence and diarrhoea, which occurred on Ismelin therapy, was replaced by sleepiness on Aldomet.
2. Dryness of the mouth and nasal stuffiness on reserpine were replaced by swelling of the face and legs on Aldomet.
3. Drowsiness on reserpine was replaced by constipation on Aldomet.

REFERENCES