sterilize cells, and the contents of an ampoule after dilution with 20 ml. normal saline was injected subcutaneously beneath wide areas of skin of both flanks, without prior addition of adjuvant. Inoculations were repeated fortnightly in each patient for 2–4 successive treatments.

Effect of Inoculation of Heavily Irradiated Autologous Tumour Cells on Survival in Ten Patients with Malignant Melanoma

Case No., Sex, Age (Site of Primary)	Survival in Months (a) Pre-inoculation* (b) Post-inoculation
1 Male 39 Ear	(a) 36 (b) 2 (dead)
2 Male 42 Leg	(a) 30 (b) 24 (alive with metastases)
3 Male 58 Shoulder	(a) 17 (b) 11 (dead)
4 Male 32 Chest	(a) 9 (b) 6 (dead)
5 Male 30 Chest	(a) 7 (b) 5 (alive with metastases)
6 Male 53 Choroid	(a) 24 (b) 10 (alive with metastases)
7 Male 50 Arm	(a) 4 (b) 24 (alive with metastases)
8 Male 63 Abdomen	(a) 60 (b) 2 (dead)
9 Female 46 Leg	(a) 5 (b) 2 (dead)
10 Female 35 Chest	(a) 18 (b) 4 (dead

* From time of treatment of primary melanoma till inoculation.

The Table shows survival times for the 10 patients, both before and after inoculation, and the results obtained are summarized as follows:

(1) Inoculations caused no systemic reactions nor local complications from infection or growth of the injected tumour.

(2) Metastases present at time of inoculation did not disappear nor decrease significantly in size. Progress of the disease did not appear altered and further metastases developed, requiring irradiation and chemotherapy to be used to attempt palliative growth control.

(3) Six patients died within six months from the disease, and four were alive at 5–24 months after inoculation, but these four all had metastases and died within a few months after the results in the Table were compiled.

In a concurrent series, 12 patients with similarly recurrent advanced malignant melanoma (six with blood-borne metastases) received treatment by radical irradiation with 4 meV x-rays in high-pressure oxygen for inoperable and recurrent lymph-node metastases, no autoimmunization being given. Six patients died within six months from their disease, four died from metastases 12, 16, 20, and 20 months after irradiation, and two were alive 24 months after irradiation (one with a local recurrence developing at 20 months, the other apparently clear of disease).

It seems doubtful if the two procedures differed in their influence on the natural history of the disease in respect to spread of metastases and probably survival. If irradiation does in any way increase survival by augmentation of an autoimmune process, it would appear that this effect was facilitated as readily by local irradiation in vivo (a practice often regarded as undesirable because depression of immunity is said to result) as by autoimmunization with tumour cells irradiated in vitro. One wonders, therefore, if irradiation of malignant melanoma in vivo was used to treat any of the patients reported on by Dr. Lewis and his colleagues, and if so whether this also causes cytotoxic antibody to appear.

It is of some interest to record that in case 3 (Table) 10^6 unirradiated viable tumour cells were inoculated subcutaneously in this patient on two different occasions at times after autoimmunization when the disease was progressing, but no "take" of tumour resulted. Aliquots of the suspension from which these inocula were taken grew rapidly in tissue culture and formed typical "heaped up" pigmented clones on subsequent passage in vitro. The patient was inoculated on a third occasion with a further 10^7 cells harvested from non-confluent growths of these cells cultured in vitro, but again the inoculum failed to grow. However, relentless progress of the disease with appearance of further metastases was taking place at the times of challenge with living tumour. One might postulate that cytotoxic antibodies become more freely available to cells injected artificially into "virgin territory" than to those distributed spontaneously by blood and lymph, but this explanation seems somewhat unsatisfactory.

These results have been essentially negative in respect to therapeutic value, and the wide variation in natural history of this disease needs to be taken into account in planning trials designed to determine the therapeutic benefits from autoimmunization in malignant melanoma.—I am, etc.,

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Rat and Human Chromosome Studies after Promazine Medication

SIR,—A number of workers have focused attention on the induction of chromosomal aberrations in vivo[1 2] and in vitro[3–6] by a hallucinogen lysergic acid amide (L.S.D.). This effect has, however, been contested by some authors.[7 8] Yet they draw attention to the possibility of some psychotropic drugs in current use inducing chromosomal aberrations.

Two recent studies[9 10] have reported the absence of a noxious effect of phenothiazines on chromosomes.

My own investigations carried out on laevomepromazine have demonstrated complete lack of abnormalities in rat and human chromosomes. The action of laevomepromazine on the chromosomes of white rats from a non-inbred batch was tested. The animals were furnished by the Cantacuzino Institute, Bucharest. A first batch of 25 animals was acutely intoxicated with a 400–600 mg./kg. body weight. A second batch of 25 animals, which served as a chronic experiment, received 50 mg./kg. body weight by mouth for 30 days. A third batch, consisting of 20 rats, served in a 30 days' chronic experiment in which laevomepromazine was used in association with Librium (chlordiazepoxide). In each case 30 metaphases, obtained from bone marrow by standard methods, were examined. In none of the cases was any change observed, neither in the number nor in the structure of chromosomes. The same negative effect was obtained by cultures of the peripheral blood from 12 schizophrenic patients who had previously had one to four years' treatment with chlorpromazine or laevomepromazine.

The negative results obtained do not exclude the possibility of actions at the molecular level. To elucidate this, more thorough and systematic investigations need to be made.—I am, etc.,

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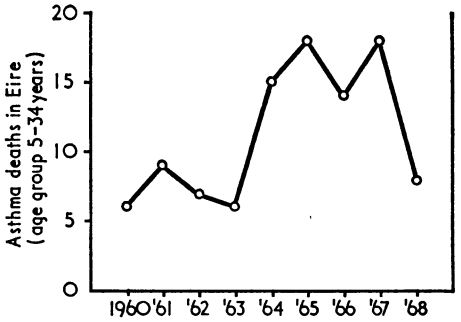
Asthma Deaths in Eire

SIR,—There has been increasing circumstantial evidence that bronchodilator aerosols used in excess have been a factor in the increase of asthma deaths in many countries.[1 2] Further evidence is presented in the graph which shows the number of asthma deaths in Eire during 1960–8 in the age group 5–34 years. This is accepted as being the most representative and suitable age group to demonstrate such an increase, which is also evident in all age groups above five years. Though the numbers are small, the increase, plateau, and decline are similar to that noted in England and Wales. The percentage increase has been smaller, 130% in Eire against about 250% in England and Wales.



1960–3=28 deaths; 1964–7=65 deaths. Increase=132%.

The important difference, however, is that the increase in the number of deaths occurred three years later in Eire. This corresponds to an approximate three-year delay in marketing bronchodilator aerosols in Eire. While they were available here in 1960, it was only in 1963 that they were prescribed in bulk. The indications are that the total sales were relatively less in Eire. In addition, sales fell in 1968 following the pamphlet issued by the Committee on Safety of Drugs in 1967, notices from drug firms, and a statement from