teasing the node apart with forceps in cold Minimum Essential Medium. Cells were then stained by the technique described by Aisenberg and Bloch.[17] All cultures had at least 95% viability by trypan-blue exclusion before staining. After staining, the cells were washed twice in cold phosphate-buffered saline, slides were prepared, and the cells were then observed by phase and fluorescence microscopy.

Only a few acceptable Reed-Sternberg cells were seen. All Reed-Sternberg cells observed, however, exhibited positive fluorescence after staining with antiserum to human immunoglobulins (Meloy). The staining patterns seen included punctate membrane fluorescence and/or a more homogeneous speckled staining of the cytoplasm of some cells. It has been my experience that Reed-Sternberg cells are difficult to obtain in suspension culture, because there are usually so few of them in the tissue, and their large size may result in loss or destruction of the cells during the process of suspending and washing them. The histological sections of this case were diagnosed as mixed-cellularity Hodgkin's disease. The sections showed a very large number of Reed-Sternberg cells, and this is probably the reason that several of them were found in the fluorescent-stained material.

Also observed in this case were a number of large cells with large, pleomorphic nuclei and large nucleoli, which were felt to be equivalent to the Reed-Sternberg " variants " and " malignant histiocytes " described in Hodgkin's disease. 78% of these cells had surface immunoglobulins. Staining with more specific antisera (anti-IgG, M, A, D, K) indicated that the immunoglobulins on these cells were limited to the IgG, K class. In contrast, 22% of the lymphocytes in this case had surface immunoglobulins, and several antibody classes were represented (IgG, M, D). Plasma cells never showed surface fluorescence, but the cytoplasm of some cells was stained homogeneously. Granulocytic cells were not stained.

Despite the fact that these cells were thoroughly washed, it is possible that the immunoglobulin on Reed-Sternberg cells in this case is exogenous, resulting from the host's immune response to neoplastic cells. However, because cytoplasmic staining was also seen, and because a high percentage of other morphologically malignant cells were also stained, I feel that this evidence may suggest a B-cell origin for the Reed-Sternberg cell.

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ASSOCIATION OF MALIGNANT MELANOMA AND MALIGNANT LYMPHOMA

SIR,—We have seen two patients with both malignant melanoma and malignant lymphoma. Aside from this interesting association, which may be related to recent observations of lymphocyte stimulation in malignant melanoma,[1,2] one of these patients presented a situation which may have important therapeutic implications.

This man was 52 years old at the time of his death in November, 1972. In October, 1963, he had noted a mole on the left forearm of many years' duration enlarge, darken, and bleed. In November, 1963, a wide excision with antecubital and axilliary node dissection was performed and the lesion was reported as malignant melanoma with negative nodes. The patient did well until May, 1970, when a mass was discovered in the left supraclavicular fossa. A biopsy revealed malignant lymphoma, lymphocytic type. Radiation therapy was given to the left supraclavicular area and to a left hilar mass. In August, 1970, a bone scan performed for increasing back pains revealed abnormal areas of uptake in several regions of the spine for which one dose of nitrogen mustard and radiation therapy were administered.

In July, 1971, recurrent nodes in the left neck prompted a series of monthly courses of cyclophosphamide, vincristine, and high-dose prednisone, which he received until May, 1972.

In June, 1972, a biopsy of recurrent left neck nodes was reported as " necrosis of lymph-nodes with organising blood clot ". Further radiation was given to the left neck. In September, 1972, a small purplish red growth appeared in the left groin, and biopsy revealed metastatic malignant melanoma. Rapid deterioration ensued and he died within 6 weeks of the appearance of the new melanotic lesion. Necropsy showed extensive melanoma with no evidence of lymphoma.

This patient remained well for 6½ years after excision of a melanoma, at which time malignant lymphoma was diagnosed. Treatment was then directed to the lymphoma, with radiation therapy and chemotherapy for over 2 years, but he succumbed to a seemingly explosive recurrence of the malignant melanoma. The possibility that the melanoma recurred as a result of immunosuppression seems likely.

Woodruff[3] described a woman who had undergone radiotherapy after a radical mastectomy three years after removal of a melanoma from the foot. Within a few weeks multiple melanomatous nodules appeared in the irradiated site and she died within a few months. He conjectured that the tumour-host equilibrium had been altered and wondered whether the melanoma cells might have remained quiescent without the stimulus of trauma of the operation or the radiography.

The present case raises many questions concerning therapy when both tumours coexist and whether " prophylactic therapy " of the melanoma with currently available drugs such as B.C.G. and imidozole carboxamide should not have been administered with the drugs given for the lymphoma.

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PROLACTIN, PHENOTHIAZINES, ADMISSION TO MENTAL HOSPITAL, AND CARCINOMA OF THE BREAST

SIR,—There is evidence that prolactin is an important factor in mammary tumour growth in certain strains of rats and mice.[4-8] The role, if any, of this hormone in human breast cancer is unclear.[9] Berle and Voigt,[10] using a modification of the local pigeon-crop test, were able to detect prolactin in plasma in 40·9% of a series of 66 patients with breast cancer compared with 8·2% in controls. Boyns et al.[11], however, using a more sensitive assay, found no difference in circulating prolactin levels between similar groups of patients. Also, Turkington et al.[12] found no detectable serum levels of this hormone in 11 patients with metastatic mammary cancer. Further, in Turkington's series, following pituitary-stalk section, 8 patients developed objective evidence of remission and in 5 of these cases this was associated with the development of high prolactin levels. On the other hand, Dickey and Minton[13]

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found that in 2 patients with advanced breast cancer, in whom levodopa decreased serum-prolactin levels, there was a remission in bone pain. Also, Salih et al.[14] and Flax et al.[15] found that prolactin alone or prolactin in combination with œstradiol or testosterone, improved the in-vitro maintenance and growth in 40 out of 130 human breast cancers. These data suggest that in some patients prolactin may be a factor in tumour growth.

Phenothiazines raise serum-prolactin levels in rats and enhance mammary tumour growth [4] though in some strains neuroleptics actually decrease tumour growth.[16] In man, both phenothiazines and tricyclic antidepressants increase serum-prolactin.[17] This has led Palmer and Maurer [18] to recommend caution in the use of such drugs in patients with breast cancer. However, Katz et al.[19] found that the mortality-rates from breast cancer between 1955 and 1961 for patients in hospital in New York mental hospitals for 10 years or more was similar to that of the general population. Presumably many of these hospital patients were exposed to phenothiazines before the development of breast cancer. Csatary [20] suggested that chlorpromazines might constitute a factor in the low incidence of neoplasia among the mentally ill. Clearly, further studies are needed to clarify these issues.

If phenothiazine provides a suitable milieu for the development of mammary cancer by increasing prolactin levels then one might expect a higher incidence of exposure to phenothiazines in patients with carcinoma of the breast than in other forms of neoplasia. We now report a preliminary investigation into this question. We have used a history of treatment in a mental hospital as a pointer to exposure to phenothiazine therapy. Patients with carcinoma of the colon-rectum have been used as a comparison group.

The names of all patients registered at the Montreal General Hospital (M.G.H.) tumour registry as new cases of carcinoma of the breast and carcinoma of the colon-rectum for the years 1966–70 inclusive were cross-checked for evidence of admission to the Douglas Hospital (D.H.), which is a mental hospital serving the English-speaking population of Quebec Province and in general would have served the population under study. Patients at D.H. requiring treatment for neoplasia would have been referred to M.G.H. for diagnosis and treatment. 9 out of 519 female patients with carcinoma of the breast had previously been at D.H., compared with only 2 out of 268 female patients with carcinoma of the colon-rectum. All these 11 patients who had been in the mental hospital had received phenothiazine therapy for schizophrenia before the development of cancer; only 2 of the breast cases were still patients at D.H. when cancer developed. Though the results suggest that there is 2·3 times as much chance of a patient with carcinoma of the breast having received phenothiazine therapy (using admission to mental hospital as a pointer to case-finding) than a patient with carcinoma of the colon-rectum, the difference is not statistically significant (using the χ^2 test with Yates's correction for continuity, $0{\cdot}50 > P > 0{\cdot}30$). However, in view of the trend of the data, larger studies along these lines are indicated.

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FECUNDITY AND INFANTILE CANCER

SIR,—With reference to your leading article (June 23, p. 1425) on transplacental carcinogenesis, the vital statistics of the United States allow us to see that declining fecundity has been associated with declining cancer mortality in infants. The decline in fecundity has been greatest in women over the age of 35, these being the ones to whom your adjective " susceptible " perhaps most applies.

The cancer-mortality rates for three age-groups [1,2] are:

Age-specific Cancer Mortality-rates

Year	*under 1*	*1–4*	*5–14*
1949	8·9	11·0	6·3
1950	8·7	11·7	6·7
1951	8·2	11·8	6·5
1952	8·5	11·6	6·5
1953	8·5	10·9	6·6
1954	8·4	11·3	6·7
1955	7·7	11·1	7·0
1956	7·9	11·0	7·2
1957	7·0	11·0	6·8
1958	6·5	10·9	6·8
1959	6·8	10·6	7·1
1960	7·2	10·9	6·8
1961	6·9	10·4	7·1
1962	6·3	9·7	6·9
1963	6·4	10·0	6·9
1964	5·8	9·2	6·6
1965	5·9	8·6	6·5
1966	5·6	8·3	6·4
1967	5·5	8·2	6·6
1968	4·8	7·8	6·3
1969	4·7	7·3	6·1

These rates are deaths per 100,000 of population in each group. The starting year is 1949, because the 6th revision of the International Classification of Diseases then came into use. For practical purposes the 6th, 7th, and 8th revisions are fully comparable, but not the 5th revision. For the year 1970 we have only a provisional rate for the age-group 0–14. This rate was 5·4 as against the provisional rate in 1969 of 6·6.[3] It seems reasonable to suppose that this further decline of 22% will appear in the final figures for each of the age-specific groups given above. In contrast to these younger age-groups, the age-adjusted rate for cancer mortality in the U.S. has been rising. It was 125·1 in 1949 and 129·7 in 1969.[1,2]

The fertility-rates, as live births per 1000 women, for four age-groups were:

Age-specific Fertility-rates

Year	*Women aged 15–44*	*Women aged 35–39*	*Women aged 40–44*	*Women aged 45–49*
1947	113·3	58·9	16·6	1·4
1948	107·3	54·5	15·7	1·3
1949	107·1	53·5	15·3	1·3
1950	106·2	52·9	15·1	1·2
1951	111·5	54·1	15·4	1·1
1952	113·9	55·8	15·5	1·3
1953	115·2	56·6	15·8	1·0
1954	118·1	57·9	16·2	1·0
1955	118·5	58·7	16·1	1·0
1956	121·2	59·3	16·3	1·0
1957	122·9	59·9	16·3	1·1
1958	120·2	58·3	15·7	0·9
1959	118·8	57·3	15·3	0·9
1960	118·0	56·2	15·5	0·9
1961	117·2	55·6	15·6	0·9
1962	112·2	52·7	14·8	0·9
1963	108·5	51·3	14·2	0·9
1964	105·0	50·0	13·8	0·8
1965	96·6	46·6	12·8	0·8
1966	91·3	42·2	11·7	0·7
1967	87·6	38·5	10·6	0·7
1968	85·7	35·6	9·6	0·6

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