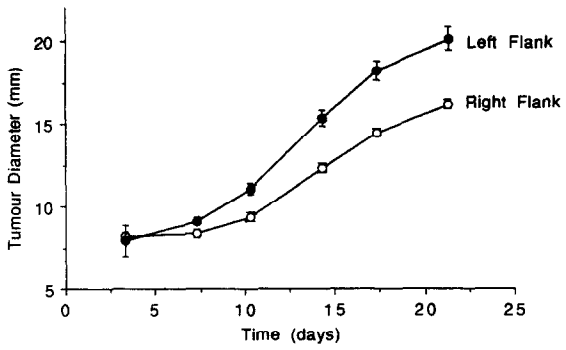


**Fig. 1. Growth curves for MKN45 tumour xenografts in left and right flanks of mice [mean (S.E.), $n$ = 10].**

tumours injected contralaterally but at the same anteroposterior levels. They suggested that the effect was due to morphogenetic gradients, similar to those believed to control differentiation during ontogeny, and they showed a similar regional difference in the growth of skin transplants [6]. We found a similar effect with human tumour xenografts, and thus we warn others considering the use of such bilateral xenografts.

1. Auerbach R, Morrissey LW, Sidky YA. Regional differences in the incidence and growth of mouse tumours following intradermal or subcutaneous inoculation. *Cancer Res* 1978, **38**, 1739–1744.
2. Auerbach R, Morrissey LW, Sidky YA. Gradients in tumour growth. *Nature* 1978, **274**, 697–699.
3. Semple TU, Quinn LA, Woods LK, Moore GE. Tumour and lymphoid cell lines from a patient with carcinoma of the colon for a cytotoxicity model. *Cancer Res* 1978, **38**, 1345–1355.
4. Motoyama T, Watanabe H. Carcinoembryonic antigen production in human gastric cancer cell lines *in vitro* and in nude mice. *Gann* 1983, **74**, 679–686.
5. Embleton MJ, Gunn B, Byers VS, Baldwin RW. Antitumour reactions of monoclonal antibody against a human osteogenic-sarcoma cell line. *Br J Cancer* 1981, **43**, 582–587.
6. Auerbach R, Auerbach W. Regional differences in the growth of normal and neoplastic cells. *Science* 1982, **215**, 127–134.

**Acknowledgement**—This work was supported by the Cancer Research Campaign, London.

*Eur J Cancer, Vol. 26, No. 6, pp. 765–766, 1990.*
*Printed in Great Britain*
*0277-5379/90$3.00 + 0.00*


# Frequency of Neurological Disease in a Cancer Hospital

## A. Hovestadt, Th.C.M. van Woerkom and Ch.J. Vecht

NEUROLOGISTS have an important role in a cancer hospital [1], but the clinical spectrum of neurological disease is not always fully realised. Probably due to both an increase in survival of cancer patients and a higher level of suspicion of neurological involvement, the frequency of neurological problems is increasing [2].

The Daniel Den Hoed Cancer Centre is one of the two cancer hospitals in the Netherlands. Most patients are outpatients. In 1988 and 1989, 7004 new cancer patients, all aged over 18, were referred for diagnosis and treatment; 1105 new patients were seen for neurological evaluation. Their tumour diagnoses were not necessarily made in these years.

Since our purpose was to evaluate the referral pattern, any change in diagnosis after the initial visit was not taken into account.

Table 1 lists for each tumour the total number of patients referred to the hospital in 1988 and 1989 and their relative frequency. The total number of patients referred for neurological evaluation and their relative frequency per tumour is included. However, the referral index (the ratio of the percentage of those referred for neurological evaluation per tumour and of the total number of patients per tumour) showed that patients with breast cancer were referred twice more frequently than were patients with lung cancer.

In breast cancer, pain was often related to vertebral or other osseous metastases and is occurred in patients in whom no other neurological diagnosis could be made. Radiculopathy secondary to vertebral metastasis or brachial plexopathy secondary to tumour involvement or radiofibrosis were frequent neurological diagnoses in breast cancer patients (Table 2). In lung cancer, brain metastasis was the most frequent neurological diagnosis. In head and neck cancer most patients evaluated for pain had recurrence of tumour with or without involvement of cranial nerves. Gastrointestinal cancer was often associated with involvement of the lumbosacral plexus, particularly by recurrence of rectal or sigmoid cancer in patients previously treated with surgery or radiotherapy.

*Table 1. Frequency of primary tumours and neurological referral*

| Tumour diagnosis | All | All | Referral index |
|---|---|---|---|
| Acute leukaemia | 122 (1.74%) | 33 (2.99%) | 1.71 |
| Bladder | 375 (5.35%) | 17 (1.54%) | 0.29 |
| Breast | 1465 (20.92%) | 327 (29.59%) | 1.41 |
| Cervix | 189 (2.70%) | 37 (3.35%) | 1.24 |
| Endometrium | 216 (3.08%) | 11 (1.00%) | 0.32 |
| GI tract | 609 (8.70%) | 64 (5.79%) | 0.67 |
| Head and neck | 668 (9.54%) | 56 (5.07%) | 0.53 |
| Hodgkin's lymphoma | 104 (1.48%) | 24 (2.17%) | 1.47 |
| Kidney | 140 (2.00%) | 32 (2.90%) | 1.45 |
| Lung | 1056 (15.08%) | 111 (10.05%) | 0.67 |
| Melanoma | 146 (2.08%) | 27 (2.44%) | 1.17 |
| Multiple myeloma | 77 (1.10%) | 26 (2.35%) | 2.14 |
| Non-Hodgkin's lymphoma | 234 (3.34%) | 58 (5.25%) | 1.57 |
| Ovary | 85 (1.12%) | 63 (5.70%) | 5.08 |
| Prostate | 442 (6.31%) | 49 (4.43%) | 0.70 |
| Unknown | 219 (3.12%) | 33 (2.99%) | 0.96 |
| Other | 857 (12.24%) | 137 (12.40%) | 1.01 |
| Total | 7004 | 1105 | |

GI = gastrointestinal.

Correspondence to Ch.J. Vecht.
A. Hovestadt, Th.C.M. van Woerkom and Ch.J. Vecht are at the Department of Neurology, Dr Daniel den Hoed Cancer Center, P.O. Box 5201, 3008 AE Rotterdam, The Netherlands.

*Table 2. Neurological diagnoses in solid tumour (by frequency of occurrence)*

| | Breast | Lung | GI tract | Ovary | Head and neck | Prostate |
|---|---|---|---|---|---|---|
| Pain | 65 | 12 | 10 | 4 | 15 | 9 |
| Radiculopathy | 52 | 11 | 8 | 2 | 2 | 10 |
| Brachial plexopathy | 44 | 7 | 1 | 0 | 5 | 0 |
| Lumbosacral plexopathy | 2 | 0 | 17 | 4 | 0 | 2 |
| Polyneuropathy | 8 | 1 | 2 | 23 | 1 | 1 |
| Mononeuropathy | 6 | 3 | 1 | 1 | 5 | 2 |
| Brain metastasis | 31 | 37 | 6 | 1 | 2 | 1 |
| Spinal cord compression | 24 | 8 | 5 | 0 | 4 | 13 |
| Encephalopathy | 6 | 10 | 5 | 3 | 3 | 0 |
| Neoplastic meningitis | 9 | 4 | 0 | 0 | 0 | 0 |
| Other | 80 | 18 | 9 | 25 | 19 | 11 |
| Total | 327 | 111 | 64 | 63 | 56 | 49 |

In non-Hodgkin's lymphoma, involvement of the leptomeninges (meningitis lymphomatosis) was the most frequent neurological diagnosis, followed by radiculopathy.

Paraneoplastic syndromes were rare: only 6 of our patients were presumed to have a paraneoplastic complication (mainly polyneuropathy and cerebellar ataxia). 161 patients, not included in the 1105 patients in Table 1, had neurological problems not related to their tumour (e.g. migraine, prolapsed lumbar disc or ischaemic brain infarction).

Since our survey was cross-sectional and not longitudinal, the figures refer only to those patients seen by the neurologist in 2 years and cannot indicate the risk of each patient developing neurological problems.

Our results show the spectrum of neurological disease to be expected in cancer patients. About 30% of patients seen by the neurologists had breast cancer. This high frequency was probably related to the long survival of patients with metastatic breast disease. Lung cancer is a frequent and well-known cause of neurological disease [3] and was the second most frequently encountered primary tumour in our series (10%). Nevertheless, the referral index (0.67) was low. Cisplatin-induced neuropathy is the cause of the high frequency and referral index in ovarian cancer. In addition almost all patients with ovarian cancer were examined as part of an evaluation of a new treatment to prevent such neuropathy [4].

A high referral index (1.72) was seen in acute lymphoblastic leukaemia. Since treatment of this disease includes prophylaxis of the central nervous system and is potentially neurotoxic, neurological consultation is often requested. In addition, leukaemic meningitis, opportunistic infection and vincristin-induced polyneuropathy may develop.

Pain was a common cause for neurological consultation. In about half the patients referred for pain, a specific neurological cause could be found (e.g. radiculopathy or plexopathy). Another common cause was osseous metastasis, usually in the spine or pelvis.

1. Gilbert MR, Grossman SA. Incidence and nature of neurologic problems in patients with solid tumors. *Am J Med* 1986, **81**, 951–954.
2. Posner JB. The role of the neurologist in the management of cancer. *Am J Med* 1978, **65**, 4–6.
3. Sculier JP, Feld R, Evans WK *et al.* Neurologic disorders in patients with small cell lung cancer. *Cancer* 1987, **60**, 2275–2283.
4. Gerritsen van der Hoop R, Vecht ChJ, Burg MEL van der *et al.* Prevention of cisplatin-induced neurotoxicity with a ACTH(4–9)-analogue in patients with ovarian cancer. *N Engl J Med* 1990, **322**, 89–94.

*Eur J Cancer, Vol. 26, No. 6, pp. 766–767, 1990.*
*Printed in Great Britain*
*0277-5379/90$3.00 + 0.00*


# Small Cell Lung Cancer Cell Line from Histologically and Immunocytochemically Negative Bone Marrow

**Michele J. Everard, Valentine M. Macaulay, Toon Min, John L. Millar and Ian E. Smith**

ROUTINE HISTOLOGICAL examination detects bone marrow involvement in 10–30% of untreated patients with small cell lung cancer (SCLC) [1], whereas immunocytochemistry with anti-SCLC monoclonal antibodies [1,2] detects SCLC cells in 40–75% of bone marrows. Carney *et al.* [3] were unable to culture tumour cells *in vitro* from any histologically negative samples, but SCLC cells have been grown from histologically negative bone marrow samples where immunocytochemistry has revealed tumour cell infiltration [2]. We report a SCLC cell line established from a bone marrow in which tumour cells were not detectable by histological and immunocytochemical criteria.

In February 1986, a 52-year-old woman presented with SCLC and liver metastases. Tumour cell infiltration was not found by routine histological examination of a pre-treatment bone marrow aspirate. Culture of a duplicate sample showed no tumour cell growth over 10 weeks. The patient underwent six courses of chemotherapy with carboplatin, etoposide and ifosfamide, resulting in a partial response. 1 month later she relapsed with meningeal involvement and a persistently low blood count. At this time (October 1986) a second bone marrow aspirate was taken. 2 weeks later the patient died. There was no necropsy.

Tumour cells were not detected by histological examination of smears and clot sections of the second aspirate. Immunocytochemistry with antibodies to epithelial membrane antigen (EMA) [4] and low molecular weight keratins (CAM5.2) [5] also failed to reveal malignant cells. A duplicate marrow sample was collected in RPMI 1640 containing 4 mmol/l glutamine and 50 U/ml preservative-free heparin, layered on Ficoll-Hypaque

Correspondence to: M.J. Everard, Department of Medicine, F Block, Institute of Cancer Research, 15 Cotswold Road, Belmont, Sutton, Surrey SM2 5NG, U.K.
M.J. Everard, V.M. Macaulay, J.L. Millar and I.E. Smith are at the Department of Medicine, Institute of Cancer Research and Lung Unit, Royal Marsden Hospital, Sutton, Surrey, U.K. and T. Min is at the Department of Cytogenetics, Institute of Cancer Research and Royal Marsden Hospital, Sutton, Surrey, U.K.