

THE YEAR BOOK
of
CANCER
1973

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THE YEAR BOOK *of* CANCER 1973

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INTRODUCTION

The development and changing areas of activity in the battle against cancer are ever-intriguing to observe. The ferment in this past year's cancer literature is as interesting as that of the past. Emphasis is being redirected to immunology and immunotherapy, to unusual refinements in diagnostic methods and tools, to new appraisals of current therapeutic methods, to continuing evaluation of the quality of life, to re-evaluating and discovering subtle variations in a single type of cancer and, hence, changing attitudes regarding prognosis. These developments appear in this YEAR BOOK OF CANCER.

Immunology and immunotherapy have now achieved another stage of maturity. In just the past year, over 1,000 oncologically oriented articles on these subjects were published. It is anticipated that there will be rapid progress in applying immunologic advances to benefit the cancer patient. There can be no doubt that the technics involved and being developed will lead to a much clearer understanding and improved control of malignant processes.

In the area of diagnostic oncology, ultrasound is receiving recognition as being a valuable diagnostic tool, particularly in aiding in the diagnosis of renal masses and in determining the involvement of abdominal structures with malignant disease. Other promising diagnostic technics include fine needle aspiration biopsy of the liver and breast xeroradiography.

New appraisals of current therapeutic methods have led to the recognition of possible hazardous effects of commonly used compounds and of some therapeutic modalities. An example of this is the warning presented about the dangers of estrogen therapy in pregnant women. There is an increasing body of evidence which indicates that girls born of mothers so treated may become victims of vaginal adenocarcinoma when they reach young womanhood. Limited surgical therapy and irradiation therapy as primary treatment of breast cancer patients are undergoing rigid evaluation, from the aspect of the type of therapy (radical as compared to nonradical) and as to whether each still justifiably can be used as a sole mode of therapy. Some authors are taking to task various recent lay reports that a major consideration in the management of mammary cancer should be the preservation of the feminine appearance; this group of authors believes that the preservation of life takes precedence and it cannot be insured by limited therapeutic measures.

The quality of life comes under closer scrutiny in the discussions of the social problems of "ostomy" patients after hospital discharge. There are interesting comparisons of the problems encountered in such patients in Great Britain and in the United States. Another social problem—the current "drug scene"—enters for the first time into the YEAR BOOK OF CANCER with a case report of a patient whose damage, almost misdiagnosed as cancer and almost resulting in amputation, was caused by the social misuse of drugs.

No longer can one assume that the long-term surviving host or cancer patient is unusual—rather it is the form of that patient's disease which is proving to be unusual. Subtle variations are being discovered about a single type of cancer, and these variations indicate that each single disease has had heretofore overlooked facets which affect prognosis. There are strong implications that there is a distinct disease—familial breast cancer—which carries with it a much higher risk of recurrence than does nonfamilial breast cancer. Similar variations are also being noted in patients with Hodgkin's disease, thyroid cancer, and lung cancer.

Such changes and developments, such subtleties and nuances, such conflicts and controversies are indications of the interest of man, researcher and clinician, in achieving victory over cancer. The 321 articles abstracted in this 17th YEAR BOOK OF CANCER were selected from about 13,400 articles appearing in the literature. As in preceding volumes of the YEAR BOOK, the selections were made by members of the editorial board; consequently the editors believe that a remarkable representation of the most important work in cancer and its related subjects is presented to the reader, in the hope that such information will ultimately benefit the most important individual in this battle—the cancer patient.

R. L. C.

R. W. C.

ACKNOWLEDGMENTS

The editors of the YEAR BOOK OF CANCER acknowledge with gratitude the excellent cooperation of the 169 members of the editorial board who contributed their time to reviewing the thousands of articles related to oncology that have appeared during the previous year. Their efforts in evaluating this vast amount of literature and their recommendations and comments on articles to be abstracted have made this volume possible.

The willingness of the more than 300 authors to prepare abstracts of their work is also greatly appreciated. Such cooperation has made possible an accurate representation of their work in abstract form. It has been especially pleasing to note that by far the majority of the authors took the time to expand the originally published abstracts of the papers and have presented detailed, concise, and updated reports.

Acknowledgment must be made of the aid given to us by the members of the staff of The University of Texas M. D. Anderson Hospital and Tumor Institute and, in particular, for their patience in answering our numerous questions. The editorial effort of Miss Dorothy U. Mizoguchi and members of the Cancer Chemotherapy Information Center of the Japanese Cancer Association is greatly appreciated.

We should like to credit the following members of the Department of Publications for their year-long endeavors in preparing the volume for publication: Miss Susan L. Huey for managing the many logistics of the volume, and Mrs. Connie C. Fox for library research.

As with preceding volumes of the YEAR BOOK OF CANCER, we wish to acknowledge the continued support of the William Heuermann Fund in the publication of this 17th book in the series.

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BRAIN AND NERVOUS SYSTEM

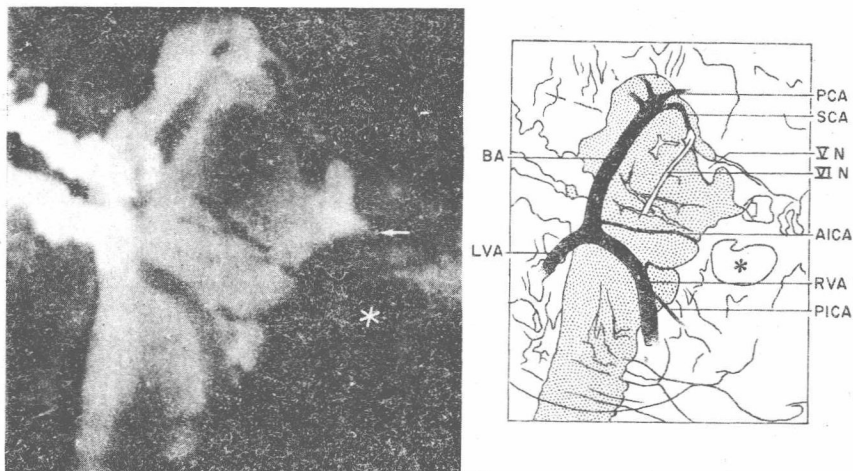
Cerebellopontine Angle Myelography. Hillier L. Baker, Jr.¹ (Mayo Clinic). Posterior fossa myelography, first described in the late 1950's, has been employed in more than 1,400 cases at the Mayo Clinic during the past decade. A precise technic for the examination has evolved, based on the necessity for complete demonstration of all cisterns in the posterior fossa and the small anatomic structures contained within the fossa.

A thorough appreciation of normal anatomy as seen roentgenographically (Fig. 1) is essential for a correct diagnosis. The various neural and vascular structures are easily recognized, but, in spite of a widely held belief that the *normal* internal auditory canal is always demonstrable, it could not be filled with contrast medium (Pantopaque) in 1% of our patients. In 10 patients in whom the contrast medium halted abruptly at the entrance to the internal auditory canal but showed no indentation of a rounded mass protruding from the porus acusticus to block its passage, a normal cistern was surgically demonstrated. Now, when we cannot demonstrate such an indentation, we reexamine the patient later; in several such patients, the original findings have remained unchanged 3 years later.

Abnormalities were encountered in only about one fourth of all myelograms of the posterior fossa (Table 1); but in patients with neurologic signs specifically localized to the pontine and cerebellopontine angle cisterns, the findings were abnormal in 35%.

Every lesion of the cerebellopontine cistern (Tables 2 and 3) had the

Fig. 1.—*Left*, roentgenogram taken with patient prone in order to demonstrate normal cerebellopontine cistern. Internal auditory canal is designated by *arrow* and the jugular foramen, by *asterisk*. *Right*, diagram of principal landmarks. SCA, superior cerebellar artery; BA, basilar artery; LVA, left vertebral artery; PCA, posterior cerebral artery; AICA, anterior inferior cerebellar artery; PICA, posterior inferior cerebellar artery; RVA, right vertebral artery; *open arrow*, internal auditory canal; and *asterisk*, jugular foramen. (Courtesy of Baker, H. L., Jr.: J. Neurosurg. 36:614–624, May, 1972.)



(1) J. Neurosurg. 36:614–624, May, 1972.

TABLE 1.—FINDINGS IN 1,422 MYELOGRAMS OF THE POSTERIOR FOSSA

MYELOGRAPHIC FINDINGS	NO. OF CASES
Negative	1059
Positive	363
Tumors	(177)
"Nontumors"	(10)
Arnold-Chiari malformation	(129)
Miscellaneous conditions	(47)
Total	1,422

TABLE 2.—ULTIMATE PATHOLOGIC DIAGNOSIS OF MASS LESIONS NOTED IN 187 MYELOGRAMS OF THE POSTERIOR FOSSA

LESION	NO. OF CASES
Neurilemoma	106
Eighth nerve	(102)
Fifth nerve	(2)
Seventh nerve	(1)
Eleventh nerve	(1)
Meningioma	18
Primary cerebellar tumors	10
Metastasis	11
Brainstem glioma	16
Cholesteatoma	5
Chemodectoma	7
Chordoma, sarcoma	2
Dermoid	2
"Nontumor"	10
Total	187

TABLE 3.—MISCELLANEOUS CONDITIONS CAUSING A MASS NOTED IN MYELOGRAMS OF THE POSTERIOR FOSSA

CONDITION	NO. OF CASES
Aneurysm	17
Vascular (hemorrhage, angioma)	9
Anomalies	7
Granuloma (adhesions)	4
Posttraumatic changes	6
Postoperative changes	4
Total	47

roentgenographic characteristics of a mass because the contrast medium was prevented from assuming a normal contour. Most of these lesions were acoustic neurilemmas, although other masses also were encountered; in most patients, the specific nature of the lesions was impossible to identify. Roentgenographically, studies with positive findings could be separated into 2 categories: those in which contrast medium (even 1 droplet) traversed the porus acusticus and entered the internal auditory canal (40%), and those in which this did not occur (60%).

In patients in whom contrast medium entered the internal auditory

canal, we encountered no tumors of the 8th nerve. Small filling defects within the canal were caused by tiny angiomas, but no so-called intracanalicular acoustic neurilemmomas were found, and the author questions the efficacy of performing extensive tomographic studies of the oil-filled canal to discover such tumors. Masses at a distance from the canal did not have any characteristic appearances that allowed exact diagnosis. Pathologic entities represented in this group included meningioma, chemodectoma, arachnoiditis, hemangioperithelioma, extra-axial brainstem glioma, subpial hematoma, and cranial nerve infarct.

Masses prevented contrast medium from entering the internal auditory canal in 60% of the cases with positive findings, but only about 70% of the lesions were acoustic neurilemmomas. Acoustic tumors often had a characteristic appearance, including bony changes, but some of the other lesions had similar findings. Meningioma, metastasis, aneurysm, and extra-axial brainstem glioma presented particular difficulties in exact diagnosis. Complete visualization of the size and position of the mass helped in selecting the most appropriate and least hazardous surgical approach.

The radiologist who performs myelography of the cerebellopontine angle should be cognizant of correct technics and normal roentgenographic anatomy. An adequate volume of contrast medium must be used to completely delineate the true extent of the pathologic changes, and caution must be used in making an unequivocal diagnosis of acoustic neurilemmoma, lest it result in an inappropriate surgical approach to a different lesion.

► [This is a useful neuroradiological investigation helpful in the early diagnosis of cerebellopontine angle lesions, especially of nerve tumors. The examiner should be aware of nontumor filling defects in this area, such as arachnoid adhesions, in reaching a final interpretation. Many, who have seen the precision and completeness of examination attainable with air combined with laminography, would challenge the claim that Pantopaque "displays normal and pathological structures more completely than any radiologic examination yet devised. . . ."—Eds.]

Evaluation of Management of Patients with Cerebral Metastases from Malignant Melanoma. Jeffrey A. Gottlieb, Emil Frei III and James K. Luce² (Univ. of Texas M. D. Anderson Hosp. and Tumor Inst.) analyzed treatment results in 41 patients with cerebral metastases from malignant melanoma to evaluate the response to whole brain irradiation with chemotherapy and/or corticosteroids. Patients received a median tumor dose of 3,000 rads delivered to the entire brain over a 2-week period using parallel opposed ports. Concomitant chemotherapy and corticosteroids were given to 24 patients; 14 others received chemotherapy or steroids. Chemotherapy consisted of dimethyl-triazenoimidazole-carboxamide alone or in combination with vincristine and bis-chloroethyl-nitrosourea.

Median and mean survivals from completion of irradiation for all patients were 86.5 and 103+ days respectively (range: 4 to 436+ days). Sixteen patients (39%) showed definite neurologic improvement and had a median survival of 131 days. Median survival of the 25 nonresponding patients was only 17 days ($p < .002$). Median duration of improvement was 60 days (range: 30 to 436+ days). Patients with metas-

tases limited to the central nervous system had a significantly longer survival than those with more widespread disease.

The most frequent responses included return of limb function; disappearance of confusion, somnolence, and coma; and cessation of headaches, nausea, and vomiting. Patients with neurologic improvement tended to have more indolent disease than those who did not respond. This study emphasizes the grim prognosis for patients with cerebral metastases from malignant melanoma.

Increased doses of radiation therapy administered with corticosteroids and new systemic chemotherapy as it becomes available may be a productive area for future research, especially in patients with rapidly advancing disease.

► [More frequent attempts to manage cerebral metastases are meeting with slight but encouraging results. Patient selection is undoubtedly an important factor in that the patient with single or more slowly progressive lesions has a more prolonged response.—Eds.]

Sterol Test for Human Brain Tumors: Relationship with Different Oncotypes. Remo Fumagalli and Pietro Paoletti³ (Univ. of Milan). Previously it was reported that desmosterol, a precursor of cholesterol, is a normal constituent of growing brain tissue of various mammalian species, including man. Desmosterol has also been found in human brain tumors of glial origin, in some transplantable murine glioblastomas, and in experimental tumors, induced by ethylnitrosourea, of the central nervous system. However, desmosterol has been found to be hardly detectable in mature human nervous tissue. The presence of desmosterol in fetal brain tissue and brain tumors appears to be related to the rate of sterol biosynthesis in these tissues. Also, desmosterol normally is absent from cerebrospinal fluid (CSF) of patients affected by nontumoral neurologic disorders, while it is detectable in some brain tumor patients.

A short treatment with triparanol (1-[p-(beta-diethylaminoethoxy)phenyl]-1'-(p-tolyl)-2-(p-chlorophenyl)ethanol), an inhibitor of the last steps of cholesterol biosynthesis, has been shown to induce a higher accumulation of desmosterol in the CSF of brain tumor patients, than in patients affected by other neurologic disorders. A sterol test for the diagnosis of brain tumors, based on the desmosterol levels in the CSF of patients treated with triparanol (8 mg./kg./day for 5 days) has been developed by the authors. This test allows a diagnosis which is correct in 77% of the patients, incorrect in 8%, and uncertain in 15%. No side effects, either immediate or delayed, were seen with the use of triparanol. The effectiveness of the triparanol treatment is assessed by determining the accumulation of desmosterol in plasma. Cerebrospinal fluid desmosterol is quantitated, using a combination of chromatographic technics. Cerebrospinal fluid (5 ml.) is freeze-dried and the residue saponified with alcoholic KOH. Total sterols are extracted with petrol ether, purified by thin-layer chromatography, and determined by gas chromatography. This test is considered positive for the presence of a brain tumor when CSF desmosterol concentrations are higher than 0.1 µg./ml., or when the desmosterol to cholesterol ratio (100 D:C) is higher than 3.

(3) Neurology 21:1149-1156, November, 1971.

CEREBROSPINAL FLUID STEROLS IN DIFFERENT BRAIN TUMOR ONCOTYPES

Tumors	No. of cases	Cholesterol ($\mu\text{g./ml.}$; mean \pm SE)	Desmosterol ($\mu\text{g./ml.}$; mean \pm SE)
Astrocytoma, first-grade	2	4.76	0.077
Astrocytoma, second-grade	7	5.12 \pm 1.07	0.116 \pm 0.022
Glioblastoma	17	17.87 \pm 4.58	0.600 \pm 0.155
Oligodendroglioma	3	4.16	0.073
Ependymoma	2	9.00	0.639
Medulloblastoma	4	4.07 \pm 1.77	0.480 \pm 0.349
Meningioma	10	22.81 \pm 8.84	1.159 \pm 0.649
Acoustic neurinoma	2	45.98	3.850
Metastatic carcinoma	7	7.76 \pm 1.46	0.145 \pm 0.041
Third ventricle tumor	2	12.77	0.364
Basal ganglia tumor	3	7.94	0.221
Hypophyseal adenoma	1	8.12	0.779
Spinal fibroangioma	1	68.51	0.851

A positive relationship between CSF desmosterol concentrations and different brain tumor oncotypes has been observed (table). Desmosterol levels higher than 0.3 $\mu\text{g./ml.}$ have been found in patients with neurinomas, meningiomas, ependymomas, glioblastomas, medulloblastomas, and 3rd ventricle tumors. A definite correlation between the concentrations of CSF desmosterol and the malignancy of the tumors has been found in the group of gliomas. First-grade astrocytomas and oligodendrogliomas have CSF desmosterol levels below 0.1 $\mu\text{g./ml.}$; 2nd-grade astrocytomas have levels just above 0.1 $\mu\text{g./ml.}$; while glioblastomas, ependymomas, and medulloblastomas have levels around 0.5 $\mu\text{g./ml.}$ The CSF desmosterol test was positive in 68 of 91 cases (74.7% correct diagnoses). The diagnostic accuracy was very high for medulloblastomas (100%), 3rd ventricle tumors (100%), basal ganglia tumors (83%), and glioblastomas (81.5%), satisfactory for 2nd-grade astrocytomas (60%) and metastatic carcinomas (62.5%), and poor for the 1st-grade astrocytomas (25%).

A correlation between CSF desmosterol concentrations and both histologic type and site of tumor growth is evident. A significant example is the increase of desmosterol levels with the malignancy of the glial tumors and the very high CSF desmosterol levels despite the low-growth rates in tumors in direct contact with the principal CSF pathways, e.g., 3rd ventricle, basal ganglia, and spinal tumors.

► [This test may be a good tool for following the course of brain tumor therapy, but further evaluation of its potential is necessary, as was mentioned by J. F. Weiss *et al.* (Neurology 22: 187, 1972).—Eds.]

Radiation Myelopathy. Jacques J. Palmer⁴ (Univ. of Washington) presents reports on a series of 12 autopsied patients, all of whom had

(4) Brain 95:109–122, 1972.