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RESEARCH EDUCATION CONTROL

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COMMUNITY CANCER CONTROL PROGRAM SURVIVES SCHMIDT CRITICISM; NCAB VOTES TO CONTINUE

Benno Schmidt, who had expressed such serious doubts about the community based cancer control program (CBCCP—formerly called the "saturation" program) that it appeared he might go all-out to kill it, gave it his best shot at the final day of the National Cancer Advisory Board meeting last week.

But when the smoke cleared, the Board voted to continue the program without change. Not only had Schmidt failed to win over the Board to his view (for perhaps the first time since he has been chairman of the President's Cancer Panel), but he reached the conclusion himself that the program has merit.

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In Brief

NCI, OMB HEADING FOR NOVEMBER CONFRONTATION OVER HAWAII, PAPANICOLAOU CONSTRUCTION FUNDS

NOVEMBER CONFRONTATION between NCI and the Office of Management & Budget is shaping up, again on the issue of funding new construction at cancer centers. The National Cancer Advisory Board has previously approved the construction grant applications from Hawaii and the Papanicolaou Institute in Miami but has not yet recommended them for payment. If the Board does approve payment, OMB either will have to back down on its refusal to release new construction funds or possibly face a lawsuit. The President has no legal authority to withhold money intended for new construction. . . . NO MORE NEW grants will be funded until the fiscal 1976 appropriation for NCI becomes final in any case, including those mentioned above. NCI had planned to fund $7 million worth of new grants during the second quarter of the fiscal year, based on a total funding level of $703 million in the appropriations bill voted by the House. NCI is operating on a continuing resolution which specifies that until a regular appropriations bill is passed by Congress and signed by the President, the lowest figure in the House or Senate bills will be the operating figure. But President Ford has submitted a deferral request, which under the year-old Budget Act he is authorized to do, cutting spending to the level of his 1976 budget request, $605 million. Either house of Congress can kill the deferral request. House-Senate conferees are scheduled to meet next week to work out their differences (the Senate voted $803 million for NCI plus training funds). Ford has threatened to veto every appropriation bill that exceeds his budget, and the HEW bill certainly will do that. However, the rider in the bill against forced busing is in line with Ford's philosophy on that issue, and could lead him to sign it despite the threat. . . . SEVEN ADDITIONAL construction grants will be going to NCAB for approval in November. They total $3 million, of which $1 million will be for new construction.

BOARD, RAUSCHER SUPPORT SAVES COMMUNITY CANCER CONTROL PROGRAM

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Immediate result of the Board's decision is that NCI's Div. of Cancer Control & Rehabilitation will proceed with awarding implementation contracts to the Univ. of New Mexico and the Michigan Cancer Foundation. Those awards were help up when Schmidt first expressed his doubts two months ago. The nine planning contracts in the program had been awarded before Schmidt had raised his objections.

DCC&R Director Diane Fink outlined the program in considerable detail to the Board and was supported in presentations by Lester Breslow, UCLA, who led the cancer control planning conference last year, and by NCAB member Gerald Murphy, Roswell Park, who is chairman of the Cancer Control and Rehabilitation Advisory Committee.

Fink noted that "There is a plethora of control components in the cancer community. Together with other factors, this results in a number of organizational and managerial problems which must be recognized in the development and implementation of a cancer control program plan of action:"

- Fragmentation – multiple organizations engaged in cancer research and control; frequently, service components are not linked and the community suffers (e.g., inadequate or no referral and follow-up after screening).
- Duplication – multiple organizations doing the same research or providing the same services, (e.g., too much screening for affluent populations, little or no screening for the poor).
- Variation – the quantity of cancer control services ranges from none to complete; the quality of service ranges from excellent to poor (e.g., treatment of leukemia).
- Dissociation – lack of communication both inter- and intra-organizationally in the control and research communities.
- Deficiency – shortages of adequately trained personnel, of facilities, and of diagnostics and therapeutic agents and equipment.
- Inconstancy – governmental (particularly federal) health support programs are "reorganized" too frequently; the net effect is to impede programs supposedly supported by these government activities.

Fink said the goal of CBCCP is to determine the efficacy of the integrated application of multiple control interventions in dealing with selected cancers through cooperative efforts in large community settings.

- The community is to identify and select three to five forms of cancer which can have a significant impact on the community for which resources are available for the application of the maximum number of cancer control interventions which are demographically important to the community and can be integrated through public and professional education and action by the community.
- The community is defined as "a natural or logical health services area." A community may include an entire metropolitan area, including its suburban and rural fringe, a segment of a large city, a large rural area including small towns and open country, or suitable combinations of these. It may comprise an entire state or a group of states. The community defined should have a population of 1.5 to 3 million.
- The community must identify all important interests of the community which relate to cancer. The leadership will be selected by the community, not the government, to act as fiscal and administrative agent.
- The population based data system will provide community surveillance, patient follow-up, monitoring of program operations, and evaluating program results.

CBCCP contracts are of two types:

a) Planning to a maximum of 18 months for maximum direct cost of $100,000–planning contracts will go to implementation following peer review.

b) Implementation to a maximum five years–50/50 cost-sharing is required. There must be provision for self-sufficient continuation at the end of five years and a contingency funding plan available in the event federal funds diminish or disappear.

Fink emphasized that CBCCP is **not**:

1. To deliver or reimburse for all treatment for all patients in the community.
2. To be an unlimited source of DCCR funding to selected contractors.
3. To redirect the total health care delivery system.
4. To organize all communities for all-out comprehensive attacks on cancer.
5. To be aimed at all forms of cancer in a community.

The program is:

1. To test in a few communities the hypothesis that the coordinated use of all interventions in dealing with certain selected cancers will have a greater impact than a fragmented and/or intervention approach.

"If this hypothesis is confirmed, then the Community-Based Cancer Control Program would be a model cancer control system that DCCR would promote for widespread application," Fink said.

In his presentation, Breslow said the concept of community-based cancer control grows out of a number of circumstances:

"1. Growing and already considerable potential for cancer control. Much cancer can be prevented, e.g. through environmental control measures. Much cancer, about one-third, is already being successfully treated; more could be.

"2. Failure to realize fully and promptly the growing potential for cancer control. For example, essentially everything we know to be important in the de-

tection and successful treatment of cancer of the cervix was known in 1945; yet it took 15 years to reach half the women in the nation, and after a second 15-year period we still have not completed the job. How long will it take to test and apply fully the available, desirable methods for control of breast cancer, currently the cause of about one-fifth of all cancer deaths among women?

"3. Recognition by Congress in the National Cancer Act of 1971 that cancer control should be a special thrust of the National Cancer Program.

"4. Clarification in a series of planning conferences of the meaning of cancer control—that it consists of intervention at every point along the origin and development of cancer where the disease can be avoided or its effects ameliorated. These include prevention, screening and detection, diagnosis, treatment, rehabilitation and continuing care, through identification, field testing and evaluation of new methods, and the demonstration and promotion of proven cancer control measures to ensure their widespread application.

"5. Fragmentation of cancer control effort in communities with resulting duplication, inefficiency and under-achievement."

Breslow cited several instances when organized community action was used successfully against major health problems—chest x-ray, registration and follow-up against tuberculosis; mobilization in California of community resources for dealing with mental retardation and mental illness; and current efforts against smallpox in Bangladesh and other countries.

"Cancer is different from tuberculosis, mental illness and retardation and smallpox," Breslow said. "From the standpoint of disease control principles, however, it is no more different from them than they are different from each other. In the case of cancer are technical means available for a substantial degree of control, not yet realized? Does community mobilization of resources offer promise of realizing much more fully than at present the potential for prevention, screening and detection, diagnosis, treatment, rehabilitation and continuing care of cancer? Are these good hypotheses and would demonstration programs be the best way to test them?

"Strongly affirmative answers to these three questions emerged from the 1973-74 conferences on cancer control and gave rise to the community-based cancer control program."

Murphy emphasized nine points in his support of the program:

1. It is only a portion of the cancer control program and is intended only to encourage groups to get together.

2. The intent is not to provide health care but to encourage organizations that do provide it to improve cancer care.

3. "I view these funds as challenge funds; it is not offering something for nothing."

4. It is not a broad program that will be supported throughout the country, but only selective demonstrations on what can be done.

5. It is not a mechanism exclusive of any health system, certainly not of comprehensive cancer centers.

6. No one has "annointed" community leaders (in determining the lead agency heading up the cooperative efforts). The communities themselves have organized, selected the leaders, submitted their proposals.

7. It is not an epidemiological, end results program, but the people/benefit ratio is self-evident in the opinion of DCC&R advisors.

8. It is not a regional program but is centralized, organized and comprehensive.

9. NCAB has multiple options, from scrapping the program entirely, permitting the planning awards to be carried out, re-reviewing the program, or permitting it to proceed as planned.

Schmidt responded with his objections. "I'm certainly most heartifuly in favor of the objectives of the program and of Dr. Breslow's desirable ends which he hopes will flow from it," Schmidt said. "It is difficult for me to find myself on the side of finding some real difficulties with this program.

"I think it may be too much too soon. There are problems not foreseen by its advocates. It may make it hard to proceed with the research, basic and clinical, that we must have if the cancer program is to succeed.

"There is too much ignorance in too many areas," Schmidt continued. "We don't have the basic knowledge to proceed to applied research. In some few areas we do. Some treatment ranges from poor to high quality. And we do want best technology applied to the most people possible.

"I have defended the role of cancer control in NCI and NIH. Some feel that no control or demonstration activities should be included in research programs. I feel we ought to be in charge of demonstrating the best and latest. In breast cancer, cancer of the cervix, the cooperative groups, we have made outstanding efforts to move the best to the bedside.

"But the premise that now, today, we can move into selected communities and see that those people get the best in cancer care, can't be implemented. To attempt to implement it and then not be able to do so could be highly disadvantageous.

"If I am wrong," Schmidt continued, "and it can be done, then there is no way it can be limited to Detroit, or New Mexico, or UCLA; and it shouldn't be. But that gets into better health care delivery, and then you're going to run into budget problems.

"If I was a congressman and saw that it worked in Detroit, I would see to it that it was implemented in my community. . . . If we don't know what the best combined modality is, we can't expect communities to implement what we don't know. . . . The concept that we can achieve better cancer care through better organization is doubtful.

"I would rather see the cooperative groups ex-

tended; our education efforts extended. . . . It worries me to try this on this scale at this time. . . I would like to work out some kind of support for a community effort that doesn't envisage taking the best cancer technology available in the best places and extend it to the community. It is a physical, resource, personnel and financial impossibility to do so at this time. . . We can't see that every cancer patient in Detroit gets the best cancer care possible."

Board Member Harold Amos supported Schmidt. "It's a Pandora's box . . . The idea of community organizations sponsored by NCI could be catastrophic," Amos said.

But other Board members expressed support for the program, as did Alan Davis, vice president of the American Cancer Society. "It would be a shame to dismantle the whole thing," Davis said. "Much planning has already been done. It's a challenge, to see if we can bring it all together."

Board Member Denman Hammond commented that "The problem is there is no effective leadership in getting communities and cancer centers together. There is technology that needs to be transferred now." Board Member John Hogness said, "It is a good program, a good concept. It would be a shame to see it die or wither now."

Schmidt backed away from opposing the entire program. "I want the RFP to allow the communities to do what they are capable of doing, not require them to do more than they are capable of. The RFP as it is requires them to provide the ultimate."

Ray Owen, member of the Cancer Panel, said, "Benno, I don't agree we should fear success (in response to Schmidt's contention that successful demonstrations would create widespread demand from other communities for NCI support of similar programs). I'm inclined to say, why not try it? At least some good should come out of it."

In the end, the opinion that counted the most was that of NCI Director Frank Rauscher, who has final authority over all NCI programs, with or without the advice of NCAB and the Cancer Panel. In one of the rare times he has differed openly with Schmidt on a major issue, Rauscher said:

"These are the major questions. Is there applicable technology available today that is not being used? Yes. Can cancer care be done better than it is? Yes, we can find some ways to do it better. Will it be prohibitively expensive? No, not with a few demonstration projects.

"I don't buy the argument that this will take funds away from basic research. Congress gave us separate authority for cancer control. Nor do I see success leading us into the delivery of health care. . . . If Congress says the same thing should be done in other communities, and says 'here's the money,' then we'll do it.

"Why NCI? Because we're the best. We can do it better than anyone else."

It appeared after debate had been completed that the Board would support the planning contracts but ask for delay of the implementation awards. Schmidt said that would be acceptable to him. Panel Member Lee Clark and Board Member Joseph Ogura suggested that the planning phase be continued.

But Board Chairman Jonathan Rhoads summarized the discussion, leading to the Board's acquiescence, at least, if not wholehearted endorsement, of continuing the program as planned.

"I sense that this is the feeling of the Board," Rhoads said. "That perhaps it is a little late to start this discussion. We would have been in a better position if the discussion occurred when the RFP was being developed. The Board feels the need is there and the resources are there for planning. The plan is looked upon as an education maneuver, to get elements of the community together. We cannot think of this as research, although it may lead to a certain amount of development. There is broad support for the idea that information aspects of the program should be emphasized, that we should develop a much better data base, and that the program serve as a guide for better future planning.

"The Board feels we should implement the contracts, that it is too late to turn back, but we should take a hard look at implementation in the future. Perhaps do it as a grant, or CREG, rather than by an RFP. The decision is the director's," Rhoads concluded.

Schmidt said, "That's all right with me," and the debate ended.

"HARVEST YET TO COME" FROM ADVANCES IN RADIOTHERAPY, KAPLAN TELLS BOARD

"Radiotherapy is still in a vital and dynamic state of development. By no means have we reached a plateau. Nor have we harvested all that can be harvested from the equipment improvement of two decades ago."

Henry Kaplan, Stanford, presented that view of radiotherapy's role in cancer treatment when he led off the National Cancer Advisory Board's session on cancer treatment last week.

Kaplan said that with today's background in radiobiology, which he said is "a vital and flourishing field," more sophisticated and exquisite use of radiotherapy in clinical trials is possible. "The harvest is yet to come in" from clinical trials exploring radiotherapy combined with surgery and chemotherapy, he said.

Better fractionation, manipulation of dose levels and of cell oxygen content, and utilization of the "fantastic degree" of radiosensitivity of some tumors are new horizons for radiotherapy, Kaplan said.

The reawakening field of hyperthermia has generated a "fantastic amount of interest," Kaplan said. He explained that increases in temperature can differentially kill tumor cells and suggested this may be

due to the different membrane structure of tumor cells which may affect heat dissipation rate. Heat and radiation used synergistically could be a very useful tool, and could possibly help slow the rate of recovery of tumor cells from chemotherapy, Kaplan said.

Kaplan referred to the work of his colleague at Stanford, Malcolm Bagshaw, and that of Morton Kligerman at the Univ. of New Mexico with pi mesons, or pions–extremely high energy radio particles. Since the pion passes through tissue without harming it, it can be directed safely through normal tissue. At the end of its flight, it is captured by the nucleus of the atom in the tissue at that point and causes the nucleus to disintegrate. Properly directed to a cancer cell, it could destroy that cell without harming normal cells. Kaplan described it as "wrapping high dose radiation around the tumor," and suggested the technique as one with great potential against inoperable, inaccessible tumors such as pancreatic cancer.

BAILAR CLAIMS ROUTINE MAMMOGRAPHY SCREENING HAZARD OUTWEIGHS VALUE

When John Bailar was director of the Cancer Control Program, before the program was elevated to division status within NCI and when it was in its first painful organizational stages, he had some serious reservations about the ambitious joint project then being developed by NCI and the American Cancer Society to screen thousands of women for breast cancer.

Bailar's objections were based on the use of mammography in the screening process, fearing that the radiation exposure might cause more cancer than it finds.

Bailar is now editor of the Journal of NCI, and handles other chores for Director Frank Rauscher. He is also doing some further studies on mammography, and last spring presented a paper on the question at the annual meeting of the American Assn. for Cancer Research. He recently expanded on the theme in a paper at a meeting of the Food & Drug Administration's Bureau of Radiological Health. Columnist Jack Anderson picked it up and, much to the chagrin of ACS and some NCI executives, gave it nationwide attention.

In his paper, Bailar said, "I regretfully conclude that there seems to be a possibility that the routine use of mammography in screening asymptomatic women may eventually take almost as many lives as it saves. Clearly, the three-way screen (the combination of mammography, medical history, and clinical examination) for the early detection of breast cancer can reduce mortality, but screening by medical history and physical examination alone will probably provide much or most of the same benefit without risk from irradiation, at least in women under some fairly high age limit."

Bailar based his conclusions on a review of the results of the study initiated in 1963 by the Health Insurance Plan (HIP) of New York in which 31,000 women were screened by mammography and physical examination. That group experienced a one-third reduction in breast cancer deaths over a five-year follow-up period. One-third (44 of 132) of the breast cancers detected in the screened group were found by mammography before the tumors were physically detectable. Only one of those 44 women died of breast cancer during the five-year period, indicating that early detection led to substantially more effective treatment.

In his paper, Bailar challenges the value of the screening program to those 44 women.

"Seventeen of the 44 had neoplasms of intraductal type," he said. "We may assume seven-year mortality rates for breast cancer to be about 20% for intraductal cancdrs and 40% for other types. Thus the expected numbers of breast cancer deaths in these screenees under normal (unscreened) conditions would be about 3.4 (20% of 17) for those with intraductal cancer and 10.8 (40% of 27) for the remainder. The average number of deaths expected in this number of breast cancer patients followed for this length of time would be about 14.2 (3.4 plus 10.8), or in whole numbers, 14, provided they were otherwise representative with respect to degree of malignancy, rate of growth, and other inherent characteristics of the malignant cells. In fact, only two deaths have occurred. The difference between 14 deaths expected and two observed, or 12 deaths, represents our best estimate of the maximum direct survival benefit that can be claimed for the inclusion of mammography in the three-way screen."

The prevention of 12 to 14 breast cancer deaths "seems to be the whole gross benefit from about 65,000 sets of mammograms for 20,000 women, Bailar contended. This is at the expense of a risk which he said, based on various studies on radiation hazards, leads to an estimate that those mammograms would cause from eight to 32 cases of breast cancer. This does not include the lesser hazards of radiation-induced leukemia or lung cancer, he said.

ACS responded to Bailar's paper and the Anderson column by charging that "the data base used by Dr. Bailar is scanty and tentative which makes further extrapolation of risk factors unreal." Arthur Holleb, senior vice president for medical affairs and research, said, "The 27 breast cancer detection demonstration projects of ACS and NCI are discovering highly curable breast cancers in the population being screened. Approximately 80% of the cancers found are stage I and offer an 85% five-year survival rate.

"Dr. Bailar, on his own, has massaged the preliminary reports of case finding in the detection projects and minimizes the significance and numbers of early

cancers found. ACS and NCI are seeing to it that radiation exposure of the screened population is being kept to the minimum needed for diagnostic purposes. The amount of radiation used does not approach the massive doses used many years ago in the studies on which Dr. Bailar rests his case."

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CM-67052

Title: *Conduct in vitro cell culture screening of new materials for antioncogenic virus related properties*

Deadline: *Dec. 9*

The Drug Research & Development Program of the Div. of Cancer Treatment is seeking the services of organizations having the necessary scientific and technical personnel and physical facilities to conduct an in vitro screen for materials having effects on the following oncogenic virus related properties:

(a) Effects on transformation of mammalian cells in culture by both RNA and DNA viruses. (b) Effects on the proliferation of RNA and DNA virus transformed cells. (c) Effects on oncogenic RNA virus associated RNA dependent DNA polymerase. (d) Effects on the phenotypic expression of a virus induced cell property to be specified by the respondent.

Assignments will encompass the propagation and maintenance of stock cell lines and viruses; preparation of test materials; recording, computation, and evaluation of results; and summarization and reporting of results as specified. Testing is to be performed according to fixed protocols to be provided by the respondent. Materials to be tested will be supplied by NCI.

Candidate organizations must have the capability to conduct cell culture screening and demonstrate evidence of general experience in standard cell culture techniques as well as specific experience in in vitro viral transformation systems and the enzymology of RNA dependent DNA polymerase.

Proposals must include evidence for personnel with appropriate training and experience and physical facilities for handling potentially hazardous biological and chemical materials. Organizations must demonstrate competence and resources for the complete screening of a minimum of 100 drugs per year in each of the test systems specified above. Proposals will be invited for a three-year incrementally funded contract period.

Contract Specialist: Daniel Abbott
Cancer Treatment
301-427-7470

RFP NO1-CP-65744-79

Title: *Induction of colon tumors in guinea pigs*

Deadline: *Nov. 28*

NCI is interested in establishing a contract for induction of colon tumors in guinea pigs. The objective of this project is to induce carcinoma of the colon in guinea pigs with known chemical carcinogens in order to provide a model to study the effects of BCG on the carcinogenesis process.

This study will be concerned with initially developing the most appropriate model system and establishing the dose response for induction of carcinomas of the left colon and rectum, and secondly administering BCG by different routes, observing the animals, performing laparatomies and injecting early macroscopic lesions with BCG.

Contracting Officer: Dennis Dougherty
Cause & Prevention
301-496-6361

Contract Awards

NCI DECIDES TO RECOMPETE FREDERICK CONTRACT IN 1977

Litton Bionetics' $18 million plus annual contract for operation of the Frederick Cancer Research Center will be recompeted next year, NCI has announced. Starting date for the new contract probably will be Sept. 26, 1977, which means Litton will have had the contract for five years, with sole source renewals negotiated each year after the initial award in 1972.

NCI executives earlier this year told ***The Cancer Letter*** (Feb. 21) they might decide to exercise their option to recompete the contract after the fourth year; the announcement for recompetition in 1977 ends that speculation.

Litton has said it will participate in the recompetition. The firm beat out a host of other organizations including most of the major commercial and not-for-profit research institutions and such corporate giants as IBM in the original competition in 1972.

Litton's profit comes primarily from an award fee based on performance, which amounted to $342,000 for the last six months of 1974.

NCI said further notice of the recompetition will be published in August, 1976. Estimated term of the new contract is five years.

Ronald Defelice is the NCI contracting officer for Frederick—phone 301-663-7148.

Recent contract awards include:

Title: Developmental studies with the 10T 1/2 cell culture assay for carcinogenesis screening
Contractor: Univ. of Wisconsin, $57,684.

Title: Clinical data retrieval services
Contractor: EG&G/Mason Research Institute, $622,000.

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Synthetic and biochemical approaches to chemotherapy of cancer
Contractor: Collaborative Research Inc., Waltham, Mass.

Title: Coordinated research and development program in cancer chemotherapy
Contractor: Arthur D. Little Inc.

ABSTRACTS OF PAPERS FROM ACS CONFERENCE ON GYNECOLOGIC CANCER

Following are the remaining abstracts of papers presented at the National Conference on Gynecologic Cancer, sponsored by the American Cancer Society. Other abstracts appeared last week in ***The Cancer Letter.*** *For information on availability of the complete papers, contact ACS, 777 Third Ave., New York City 10017.*

USE OF DIAGNOSTIC ULTRASOUND IN TROPHOBLASTIC NEOPLASMS AND OVARIAN TUMORS – *Mitsunao Kobayashi, Defense Medical College, Japan*

Although diagnostic ultrasound has much to offer in uterine, ovarian and other pelvic tumors, the trophoblastic neoplasms and the ovarian tumors are perhaps the best two indications for diagnostic ultrasound. Therefore, the author will confine his presentation to these conditions.

An analysis of diagnostic accuracy, differential diagnoses and diagnostic pitfalls is made in over 100 cases of hydatidiform mole thus far examined. Ultrasound has proved to be useful not only in the diagnosis of hydatidiform mole but in the followup of postmolar patients. During the course of routine postmolar followup, a sudden increase in the intrauterine echoes along with elevating urinary HCG titers was characteristically seen in patients who developed invasive mole or choriocarcinoma.

A comparative evaluation is made between the ultrasonographic and pathological diagnoses in over 400 cases of various ovarian tumors and an attempt is made to differentiate benign from malignant ovarian tumors.

THE STILBESTEROL-ADENOSIS-CARCINOMA SYNDROME – *Howard Ulfelder, Harvard Medical School*

This disease complex is one of the few entirely new and previously unsuspected discoveries of the recent past. The first case, seen in 1966, ushered in an era of suspicion. A study and report on the first seven cases published in 1969 inaugurated the era of hot pursuit which culminated in 1971 in an epidemiologically structured and controlled investigation of possible etiological factors.

With the establishment of the Stilbesterol association there was initiated a registry of cases, ushering in the era of verification. This registry, while accelerating and embossing confirmation of the suspected relationship, served an even more useful purpose by collecting under one roof and in front of one cluster of observers all the necessary and relevant data on a sufficiently large number of cases to enable rapid (1973-1974) wide dissemination of knowledge about the occurrence and behavior of the disease and its response to treatment.

The present status of the syndrome will be described in terms of histopathology, estimated prevalence and the results of treatment. Pertinent associated benign and premalignant factors will be similarly discussed. A closing commentary will draw attention to the significance of these discoveries for embryology, teratology, and carcinogenesis, and the research opportunities which offer themselves in this connection.

EARLY INVASIVE DISEASE OF THE CERVIX – *Hervy Averette, Univ. of Miami*

Probably the most controversial neoplastic lesion that concerns the gynecologist and pathologist at the present time is microinvasive carcinoma of the cervix. Although many studies have attempted to describe the lesion and its proper treatment, a precise definition that is acceptable to the majority of those concerned with the diagnosis and treatment of cervical cancer does not exist. Even the revised 1974 International Staging of Cervical Carcinoma defines microinvasive carcinoma only as "Stage IA – early stromal invasion."

At the Univ. of Miami School of Medicine we have had an interest in "superficially invasive" carcinoma since the early 1960s. It has been our policy to study and define lesions as "microinvasive" (stage IA) or "frankly invasive" (stage IB) based upon (1) millimeters of squamous cell penetration into the stroma beneath the basement membrane, and (2) the presence or absence of vasvular involvement by malignant cells. A review of the pertinent literature and personal experience with microinvasive carcinoma will be presented.

A ROLE FOR PARAPROFESSIONALS – *Duane Townsend, Univ. of Southern California*

Over the past eight years, trained registered nurses and licensed vocational nurses have been given spec-

ific responsibility in the detection and evaluation of patients with gynecological malignancies. During this period of time these paraprofessionals have been responsible for screening over 20,000 women for gynecological and pelvic malignancies. In addition to the detection of early genital tract malignancies, these same individuals have been utilized in the evaluation of over 5,000 patients with abnormal Papanicolaou tests. In addition, the evaluation of the Gravlee Jet Washer for the detection of endometrial diseases was a primary responsibility for these same individuals.

The paraprofessional works with the physician thereby providing the physician the opportunity to spend less time in detection but more time in the evaluation of the patient's malignancy and more time explaining to the patient the type of therapy needed to eradicate her problem. In addition to an extremely efficient and inexpensive system for evaluation of the patient with an abnormal Papanicolaou test, patients develop an unusual trust for the paraprofessionals which then is utilized to reinforce the physician's recommendation for therapy. It has been determined that the low income minority individual prefers a female paraprofessional for initial contact and the patient is more likely to return for further examinations as well as therapy because of the rapport established by the paraprofessionals.

LAPAROSCOPY AND HYSTEROSCOPY IN GYNECOLOGICAL CANCER – *Robert Neuwirth, Columbia Univ.*

Endoscopic techniques have only recently achieved sufficient technological sophistication to become common adjuncts to clinical diagnosis. Colonoscopy, gastroscopy and bronchoscopy are well known examples. The area of gynecologic endoscopy has undergone similar growth in sophistication so that the classic method of culdoscopy is now supplemented by laparoscopy and hysteroscopy.

Laparoscopy as now practiced utilizes fiberoptic lighting, standard optics and specialized pneumoperitoneum equipment for satisfactory performance. It is a method applicable to many gynecologic problems but the adnexal mass, the diagnosis of the etiology of ascites, and second look after ovarian cancer therapy have been some of the applications to date.

Hysteroscopy as a practical technique is only now becoming established. Already, however, there are several reports on its usefulness in the staging of endometrial cancer. Perhaps the widest application of diagnostic hysteroscopy will be as an adjunct to the curettage in abnormal uterine bleeding. With more experience, the role of this new technique will become more defined.

BIOPSY TECHNIQUES – *William Creasman, Duke Univ.*

The accessibility of the cervix has lent itself to cytologic and biopsy diagnostic techniques which have proved successful in not only identifying a lesion but discovering it at a preclinical, preinvasive stage. Current data indicates that over half of all carcinomas of the cervix are stage 0 (carcinoma-in-situ). The death rates, as well as the incidence for cervical carcinoma have, therefore, decreased over the recent decades. As a result, carcinoma of the body of the uterus is about 1½ times more frequent than cervical disease. It appears that this is a true increase in incidence for corpus cancer and not necessarily related to an enlarging overpopulation. Although relatively accessible to early diagnosis, progress in developing techniques for identifying cancer in the uterus has not been successfully developed and dilatation and curettage remains the prime diagnostic procedure. If definitive diagnosis can be established short of hospitalization and a surgical procedure, then the patient would benefit in regards to time, convenience and cost.

Cervical cytology has been less than 50% effective in diagnosing intrauterine disease. New cytologic and histologic techniques have been developed which appear to be as effective in establishing the diagnosis of corpus cancer as dilatation and curettage. These techniques will be discussed in detail.

HUMAN CHORIONIC GONADOTROPIN – *Donald Goldstein, Harvard Medical School*

One of the most exciting and useful developments in modern oncology has been the recognition that certain biochemical tags can be used as cell markers in diagnosis, monitoring the effects of anti-tumor therapy, and followup to detect tumor recurrence. The measurement of human chorionic gonadotropin (hCG) in women with choriocarcinoma and related gestational trophoblastic tumors was the first test which could be relied upon for this purpose. Furthermore, the amount of viable tumor tissue could be approximated by determining the production rate of this hormone which is always produced by trophoblastic cells.

The measurement of hCG is now similarly utilized for the management of patients (both male and female) with non-gestational choriocarcinoma originating in the testis and ovary. More recently a wide variety of non-trophoblastic tumors have also been shown to secrete hCG, presumably from primitive tumor cells. Work is currently under way to ascertain the extent and potential usefulness of this observation in a wide variety of tumor systems in the hope that improved tumor monitoring might be achieved.

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