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VIRUS CANCER PROGRAM INCLUDES "SOME OF THE BEST BASIC RESEARCH ANYWHERE," MOLONEY SAYS

Members of the scientific community who have fought the growth of targeted research support by NIH generally use NCI's Virus Cancer Program as the biggest and most visible example of how targeted research drains money and investigator talent away from basic research.

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In Brief

OMB WITHDRAWS FROM FIGHT OVER FUNDING NEW CONSTRUCTION, TOSSES THE BALL TO TED COOPER

CHALK UP a partial victory, at least, for the Cancer Program over the Office of Management & Budget. The White House has decided to let Asst. Secretary of Health Ted Cooper have the final say on whether or not new construction grants approved by the National Cancer Advisory Board will be funded. Until now, OMB has stuck with the doctrine imposed by President Nixon that no money would be released for building new health facilities. That's contrary to law, as written in the National Cancer Act, which gives that authority to the NCI director. It also violated instructions by Congress in appropriations bills. OMB was forced to back down on several occasions by pressure from Congress and threats of lawsuits. It wasn't total capitulation by OMB—the law doesn't say anything about the assistant secretary, the secretary, or even the President as having any authority over decisions to support construction of new cancer facilities. OMB's withdrawal should be a big improvement, however. Not only is Cooper more attuned to the needs of the Cancer Program but he doesn't have the history of ignoring or subverting the law that has marked the Nixon-Ford budget office. . . . **THE MOVE** was meaningless, for the present. No money will be available for any new grants, construction or research, until the 1976 HEW appropriation has been determined. House and Senate Democrats are confident they can override the President's veto when the vote comes up Jan. 27. It probably will be close, particularly in the House. . . . **AN NCI PHONE** book has been prepared by the Office of Cancer Communications and will be sent to Cancer Program constituents, making it easier to get in touch with the right person when you have a problem with or need information from the Institute. OCC Director Paul Van Nevel said he hopes the book will help spread the calls around a little more, take some of the pressures off better known staff members. . . . **ONE YEAR** from now the National Cancer Act will be up for renewal again. The NCAB sometime this year will develop its recommendations for changes and other groups will be preparing theirs. Now is the time to get suggestions in, to NCAB, NCI Director Frank Rauscher, or to organizations which will submit proposals to Congress, such as the American Cancer Society, the Candlelighters, and the Citizens Committee for the Conquest of Cancer.

HIGH QUALITY OF BASIC RESEARCH IMPRESSED MOLONEY AT VCP MEETING

(Continued from page 1)

That attitude ignores the fact that funds for basic research have increased at a dramatic rate at NCI and to a lesser extent elsewhere at NIH while Congress has continued to earmark money for VCP. More importantly, according to VCP Director John Moloney, "some of the best basic research going on anywhere" is being supported by his program.

"For instance, we have some fine basic research in molecular biology, using the virus as a handle. We're learning about the nature of cell transformation."

The high quality of basic research in his program was the most impressive factor coming out of the annual meeting of VCP contractors in Hershey, Moloney said. A portion of that meeting was devoted to reports on vaccine development (still quite some way down the road, was the consensus), but most of the time was spent on reports involving basic research.

Moloney offered as examples of VCP basic research reports on the following projects involving both in-house NCI scientists and VCP contract investigators:

Separation of Sarcoma Virus Specific and Leukemia Virus Specific Genetic Sequences of Moloney Sarcoma Virus – ***Edward Scolnick, Paul Peebles and Wade Parks, NCI; Richard Howk and Anthony Anisowicz, Meloy Laboratories; and Charles Scher, Boston Children's Hospital.***

RNA-containing mammalian type-C viruses, which are defective for replication and which produce morphological transformation of fibroblasts in cell culture have been isolated from murine, feline, and primate hosts. Two isolates of such defective RNA tumor viruses, the Moloney sarcoma virus and Abelson leukemia virus, have been obtained by passage of Moloney murine leukemia virus (Mo-MuLV) in BALB/c mice; these viruses provide an excellent model system in which to investigate the question of the universality of the nucleic acid sequences which code for transformation of different types of cells.

From the Moloney sarcoma-leukemia complex, two forms of the Moloney sarcoma virus (Mo-SV) genome have been isolated free of leukemia virus in transformed "nonproducer" cells. One of these forms of the Mo-SV genome was isolated by injection of the sarcoma-leukemia complex into hamsters; this form of Mo-SV codes for no known structural proteins of Moloney leukemia virus and thus is referred to here as Mo-Sv p^-. The other form of Mo-SV, isolated in cell culture from the sarcoma-leukemia complex, was called the S^+L^- strain of Mo-SV. This form of Mo-SV was later found to contain, as a part of its genome, information which codes for the p30 protein of Moloney leukemia virus, and thus is referred to here as a p30 positive strain of Mo-SV (Mo-SV $p30^+$). In past experiments each of these forms has been shown to be genetically stable, and each of these forms of Mo-SV is defective by itself for replication. When the Mo-SV p^- form is rescued by replicating murine leukemia virus, the complex causes sarcomas when injected into animals.

The Abelson leukemia virus, isolated by passage of Mo-MuLV in prednisolone treated BALB/c mice, can also transform fibroblasts or other cells in cell culture but produces B-cell and null cell leukemias, not sarcomas, when injected into mice. Like Moloney sarcoma virus, the Abelson genome has been isolated free of replicating helper virus, in transformed nonproducer cells. Analysis of such nonproducer cells for Moloney murine leukemia virus structural proteins has not yet been reported.

Since no molecular explanation of the biological difference between Moloney sarcoma virus and Abelson virus is available, we began nucleic acid hybridization experiments to compare the genomes of the two replication-defective viruses. As in past studies, we have done this by studying the RNA of several heterologous nonproducer cells transformed by each of these replication-defective viruses. This approach has allowed us to study the expression of the genome of the replication-defective transforming viruses in the absence of contanimating replicating helper virus. To do this, we fractionated by absorption cDNA probes from Moloney MuLV into two distinct, nonoverlapping, portions of the Moloney leukemia virus genome. Using these probes, we have found that cells transformed by the Abelson genome contained RNA homologous to a distinct portion of Moloney murine leukemia virus. This RNA in Abelson transformed nonproducer cells is largely similar but not identical to the Moloney leukemia virus sequences in the RNA of nonproducing cells transformed by the p^- strain of Moloney sarcoma virus.

In addition, a cDNA fraction has been prepared which detects in the $p30^+$ form of Moloney sarcoma virus and in cells transformed by either form of Mo-SV, RNA which is not contained in cells producing Moloney murine leukemia virus, or in cells producing N-tropic or xenotropic strains of murine type-C virus isolated from BALB/c cells. This sarcoma virus specific genetic information is not detected in RNA in cells transformed by the Abelson viral genome.

Activation of an Endogenous Mouse Type C Virus by UV-irradiated Herpes Simplex Virus Types 1 and 2 – ***Berge Hampar, Stuart Aaronson, Stephen Showalter and Claire Dunn, NCI; and Jeffery Derge and Mrinal Chakrabarty, Flow Laboratories***

Cells of many, if not all, mammalian species contain repressed genomes of type C RNA viruses. Activation of these repressed genomes with resultant virus synthesis may occur spontaneously or may be induced by biological, chemical, or physical means. Evidence exists to suggest that the genomes of these vertically transmitted endogenous RNA viruses can

play a role in spontaneous tumor induction.

Viruses containing DNA rather than RNA genetic material have also been implicated in the oncogenic process. Inoculation of herpesviruses into animals or cells in culture, for example, may be followed by the appearance of tumors or cell transformants which possess malignant potential. The putative role of herpesviruses in the oncogenic process is not clearly understood however, and one may question whether the herpesvirus genome is in itself oncogenic or whether herpesviruses serve an indirect function by affecting a cellular factor(s) which is the direct oncogen. An axample consistent with an indirect role in oncogenesis would be modification of expression of endogenous type C virus information following herpesvirus infection.

The findings here indicate that UV-irradiated HSV types 1 and 2 can activate an endogenous mouse xenotropic type C virus. Although the levels of type C virus activated by HSV were relatively low and detection required sensitive techniques, the results proved reproducible in two laboratories.

Studies of viral and chemical cocarcinogenesis are supported by VCP. Two reports follow:

DNA Related to the Transforming Gene(s) of Avian Sarcoma Viruses is Present in Normal Avian Cells and Transcribed after Chemically-induced Transformation – ***D. Stehelin, H.E. Varmus and J.M. Bishop, Univ. of California (San Francisco); C. Moscovici, VA Hospital, Gainesville, Fla.; and P.K. Vogt, Univ. of Southern California***

DNA from normal chicken cells contains nucleotide sequences closely related to at least a portion of the transforming gene of avian sarcoma viruses; similar sequences are present in the DNA of other avian species and diverge according to phylogenetic distances among the species. These nucleotide sequences are not transcribed in normal avian fibroblasts, but they are transcribed in transformed fibroblasts derived from sarcomas induced in quails with a chemical carcinogen.

The transforming gene of avian sarcoma viruses apparently evolved during the speciation of birds and was acquired by the viral genome from a normal avian cell; an analogous gene may be involved in chemical oncogenesis.

Prevention of Viral-Chemical Co-carcinogenesis in Vitro by Type-Specific Anti-Viral Antibody – ***Paul Price, Teresa Bellew, and Martin King, Microbiological Associates; Aaron Freeman, Children's Hospital, Akron; Raymond Gilden, Flow Laboratories; and Robert Huebner, NCI.***

We have previously described a Fischer rat embryo cell line which at a low passage level (less than 60), requires either the addition of an exogenous type C RNA virus or treatment with a halogenated pyrimidine prior to treatment with a chemical carcinogen in order for transformation to occur. At passage levels higher than 60, chemicals known to be carcinogenic in animals do on occasion transform the cells without preinfection by type C RNA virus. These high passage cells appear to be negative for infectious type C RNA virus; however, the gs-1 antigen of RaLV (the endogenous type C RNA rat virus) is often expressed after transformation and the rat type C virus can be induced in both the low and high passage cells by 5-iodo-2'-deoxyuridine (IdU). We have recently shown that two agents which inhibit this induction by IdU, namely, streptonigrin and cordycepin, protect the rat cells from transformation by the polycyclic hydrocarbon 3-methylcholanthrene (3MC). We report here that low passage Fischer rat embryo cultures chronically infected with the Rauscher murine leukemia virus (RLV) are protected from transformation by 3MC if treated with neutralizing antibody specific for RLV; the cultures were not protected by neutralizing antibody specific for the B-tropic radiation leukemia virus (RadLV) which is Gross-like in its neutralizing antigenic determinants.

At the first meeting of the new Virus Cancer Program Advisory Committee, one member suggested that the program "should not rest on whether or not viruses have an etiologic role in cancer, but that the study of viruses is vital in understanding cancer." However, one goal, if not the major goal, of the program remains the prevention of cancer through development of vaccines. Two reports in that area follow:

Problems a nd Potentials for Human Viral Cancer Vaccines – ***Maurice Hilleman, Merck Institute for Therapeutic Research***

Viral etiology in human neoplasia is yet to be established, but studies of comparative oncology in animals provide a basis for belief that much if not all cancer of man is caused directly or indirectly by viruses, both of DNA and RNA type. It is possible that a portion if not a majority of cancer in man can be prevented by use of viral vaccines, killed or live, such as have already been shown effective in animals, especially Marek's disease of chickens.

Studies of vaccines against cancer viruses may proceed with a rich background of prior technology obtained in the development of vaccines against ordinary acute lytic viral infections but it will be essential that current procedents and legal concepts for viral vaccines be altered if progress is to be made. Even though viral etiology in human cancer is unproved, it is timely to conduct conceptual and experimental probes in studies in animal model systems which can be applied to man when the proved cancer viruses are reliably propagated in the laboratory.

Perhaps the greatest hurdle in human cancer vaccine development, disallowing an unanticipated breakthrough, will be the establishment of safety and efficacy in a disease in which the incubation period

may exceed a half century. Progress toward a vaccine for routine use in man must necessarily, therefore, be reckoned in decades rather than in years. The road to vaccine control may be long and the way may be hard but the benefit should be worth the effort in this disease which is the cause of death in 20% of the population.

Suppression of Type C RNA Virogenes by Type Specific Oncornavirus Vaccines: Prospects for Prevention of Cancer – ***Robert Huebner, William Lane, Roy Trimmer and Paul Hill, NCI; and Raymond Gilden and Robert Toni, Flow Laboratories***

Immunization of crossbred and F_1 mice with combined killed and live GLV-AKR type C viral vaccines suppressed up to 4 logs of endogenous N type AKR virus for significant periods during early life. Since several previous studies in the same and similar crossbred systems revealed direct correlations between low and high levels of type C virus early in life with low and high incidences of leukemia and other cancers later in life, we believe that prospects for suppression of spontaneous neoplasms are good; however 8 to 14 months will be required to achieve the final results. Should cancers be prevented by serotype specific vaccines, such evidence would provide conclusive proof of endogenous viral etiology.

In addition to the $50 million Virus Cancer Program, which is in the Div. of Cancer Cause & Prevention, virus research enjoys major support through traditional research project grants, program projects and centers, stipends and salary support awards and training grants from the Div. of Research Resources & Centers. In fiscal year 1975, DRRC distributed $29 million through those mechanisms.

DCCR has described its Viral Oncology Program as follows:

In general, the program of grant-supported research emphasizes the biology of cell-virus interaction, the nature and mechanism of virus-induced neoplastic transformation and the alterations in the cell that characterize it as neoplastic. This emphasis broadly serves to distinguish the grant-supported from the complementary contract-supported program which focuses on the role of viruses in human cancer.

The identification of viral genes and their products which are responsible for neoplastic transformation and for the maintenance of the transformed state are primary targets in viral oncology for the future. It is desired to learn how these genes or their products interact with cellular components, especially cellular genes, and which cellular genes are so involved. The consequences of these interactions on the appearance of new cellular functions are further objectives of this program.

Since there is evidence that alterations at the cell surface are crucial in changing the behavior of a cell from normal to neoplastic, the cell surface is under particular scrutiny in this regard. The altered cell surface may furthermore provide antigenic or other substances useful for the diagnosis and possibly prevention or treatment of cancer. Efforts to induce transformed cells to differentiate or otherwise favorably alter their malignant properties will also be encouraged. Workshops on various aspects of those subjects will be useful to help focus on the important issues involved in these matters.

Because of their intimate interaction with cellular components and because they provide a handle which permits one to follow these reactions, tumor viruses are basic tools to study how and why certain genes of a cell are expressed and others repressed, and thus how various functions of the cell are controlled. Such studies are vital to understanding of neoplastic transformation, which, of course, results in new cellular functions. Still another goal in viral oncology is to determine the function of tumors as carriers of cellular genetic information, particularly oncogenic information of cellular as opposed to viral origin.

Guidelines for Referral of National Cancer Institute Grant Applications

The Viral Oncology Program consists of cancer virology and basic and supportive investigations.

Cancer Virology

This segment of the program emphasis viruses as tumor-inducing agents and concerns biological, biochemical and physical investigations of actual or potential oncogenic viruses, their interactions with and effects on their hosts at all levels of biological organization, i.e., molecular, cellular and organismal. It includes, but is not limited to, the following kinds of investigations: the occurrence, purification, physical, chemical, genetic, antigenic, and biological characterization of tumor-inducing viruses, their precursors and mutants, preferably those of man and the higher animals; the development of methods for their detection and assay; identification of target cells; interaction of tumor viruses with these or other cells to induce morphologic, oncogenic, cytopathic, antigenic, biochemical or other alterations of the cell on its surface and elsewhere, and the detailed analysis of these alterations; the search for mutant cells with altered responses to oncogenic viruses and the identification of the altered function; mechanism of synthesis of viruses and mode of transmission; factors (genetic, hormonal, immunological, etc.) involved in resistance and susceptibility of cells and hosts to tumor viruses; physiologic, immunologic, serologic and pathologic effects on man and animals, including the nature, histogenesis, and pathogenesis of the neoplastic diseases they induce; preparation of antigen substances from viruses or viral-altered cells for the purposes of vaccination, diagnosis or treatment; and, finally, investigations of methods to prevent, diagnose and treat actual or suspected viral neoplasias.

The mere use of standard lines of normal and virus-transformed cells in model biological investiga-

tions of divers kinds does not necessarily identify such projects for the Viral Oncology Program though, of course, does not disallow such a determination. In general the emphasis of the program is on the dynamic relationship of the tumor viruses to the oncologic process, development and expression, and applications from these considerations.

Basic and Supportive Investigations

Research on gene expression and other cell regulatory functions, utilizing viruses as tools, may be considered appropriate for the Viral Oncology Program, provided the relationship to neoplasia is clearly indicated and documented. While the greatest interest resides in the biology of animal systems, including human, projects which involve other forms of life, if these offer unique advantages and their pertinence to neoplasia documented, may also be considered for the Viral Oncology Program.

The following examples represent areas of interest in this segment of the Program: reversal or suppression of transformed cells, by biological, chemical, or physical means and the mechanisms by which this is achieved; mechanism of genetic recombination; mechanism of integration (and excision) of viral or other genetic information with (or from) cellular genes; mechanism and regulation of transcription, especially of viral genes and of cellular genes modified or influenced by viruses; mechanism and regulation of translation, especially of viral information or viral-coded information; transmission of cellular information by viruses; influence of virus infection on normal cell structures and functions.

Guest Editorial

POWER SHIFT TO COMMUNITY HOSPITALS NOTED; CENTERS MUST WORK WITH THEM

As the evidence mounts that combination therapy (i.e., surgery, radiotherapy, chemotherapy, possibly immunotherapy) may be of value (even in relatively early cancers to attack potential microscopic disseminated disease), there is almost certain to be a large national push to include the vast majority of patients with cancer in some protocol or another both for the purpose of clinical investigation as well as for therapy. This need for large numbers of patients with early cancer to enter multidisciplinary protocols will stimulate NCI and its highly subsidized cancer centers to yield some power and money to community hospitals where the vast majority of early cancer patients are treated.

It is important that those involved in cancer programs in community hospitals recognize this power shift and utilize it in the best interests of their patients. Community hospitals jointly can demand arrangements that are attractive to them and their patients. If they cannot make satisfactory arrangements with one "cancer center", they should turn to another. Since physicians in community hospitals make most of the therapeutic and referral decisions for their patients and since the number of protocols for clinical investigation has skyrocketed, the community hospital should now become a respected partner in cancer care.

Both community hospitals and cancer centers must recognize this shift in power and work out reasonable strategies to work together. Like the oil producing countries, the community hospitals will gain the most for themselves and their patients by banding together. Such organizations as the Assn. of Community Cancer Centers and the New York State Cancer Programs Assn. should help their constituents devise strategies and guidelines to deal with the cancer centers. Also the cancer centers must be willing to yield gracefully some of their previous absolute control over monies and policies to the community hospitals.

Finally, if the community hospitals cannot make reasonable arrangements with a given cancer center, NCI should deal with them directly (preferably with groups). — Reprinted from the *Newsletter on Cancer,* Charles D. Sherman Jr., Editor

ACCC TO DISCUSS PERSONNEL, FUND SOURCES, CLINICAL INVESTIGATION

The annual meeting of the Assn. of Community Cancer Centers in Jacksonville, Fla. Jan. 31-Feb. 1 will feature presentations and discussion on the expanding role of cancer care personnel, components of a community cancer program, funding sources for community cancer programs, and the principles of clinical investigation.

R. Lee Clark, president of the Univ. of Texas System Cancer Center and of the Assn. of American Cancer Institutes and member of the President's Cancer Panel, will deliver the keynote address on "Clinical Cancer – The Role of AACI and ACCC."

The North East Florida Cancer Program, a group of 31 community level cancer researchers, is host for the meeting. Van Etten Bent is president of the Florida group, and John Nelson of the group is chairman of the meeting.

The discussion on the expanding role of cancer care personnel will be chaired by Abraham Brickner, director of community programs for the Michigan Cancer Foundation. Participants will include Beatrice Reister of the Wilmington (Dela.) Medical Center on the clinical nurse specialist; Saundra Lange, nursing coordinator for the Michigan Cancer Foundation, on the home assistance nurse; Patricia Porcher, North East Florida Cancer Program, on the enterostomal specialist; and Sharon Klein, director of patient services and rehabilitation for the Michigan Cancer Foundation, on multiple roles of the social worker in the cancer program.

J. Gale Katterhagen, of Tacoma General Hospital

who is ACCC vice president, will chair the discussion on components of a community cancer program. Participants include Karl Jonas, Doctors Hospital (Washington D.C.), on the cancer program in a private metropolitan hospital; Alan Schroeder, Oncologist Medical Group (Santa Rosa, Calif.), on development of a community cancer program in a rural hospital; Jack Hartmann, Fred Hutchinson Cancer Center (Seattle) on cooperation between a community cancer center and a comprehensive cancer center; and Alan Davis, American Cancer Society vice president for public affairs, on relationship and cooperation of the local ACS chapter and the community cancer center.

David Johnson, Deaconess Hospital (Evansville, Ind.), will chair the panel on funding sources; participants include H.G. Pearce, Blue Cross Assn. senior vice president, on funds available from the Blues; Melvin Blumenthal, Social Security Administration, on Medicare and Medicaid; and Jonathan Rinehart, New York City, on philanthropy.

Gordon Zubrod, director of the comprehensive cancer center at the Univ. of Miami, will lead the discussion on principles of cancer clinical investigation. Zubrod was instrumental in the development of those principles when he was director of NCI's chemotherapy program and later of the Div. of Cancer Treatment. Charles Vogel, Univ. of Miami, will talk about breast cancer protocols, and Francisco Tejada, also of the Univ. of Miami, will discuss general protocol compliance.

James Donovan, ACCC president, said that NCI would conduct a site visit Jan. 30, prior to the start of the meeting, on ACCC's grant application to investigate ways in which community cancer centers and private physicians can participate in the national cancer research effort.

Registration forms may be obtained by writing to ACCC, P.O. Box 30279, Bethesda, Md. 20014, or by calling ACCC program coordinator Marion Cernansky, 301-656-3987.

DIET, NUTRITION COMMITTEE TO SELECT PROJECTS FOR $6 MILLION IN CONTRACTS

The Diet, Nutrition & Cancer Program Advisory Committee will meet Jan. 13 and 14 to sift through $10 million in projects developed in a series of workshops late last fall. The committee will be asked to select from a list of several dozen projects and establish priorities which NCI will use in drawing up RFPs.

Gio Gori, director of the program, said fiscal 1976 money of from $6 to 6.5 million would be available to support the contracts. Gori previously had suggested that a substantial part of the program could be funded through the CREG (cancer research emphasis grant) mechanism. However, it takes about 14 months to move a CREG project from inception to award, so that is out of the question as far as 1976 money is concerned. Contract awards can be completed before the 1976 fiscal year ends Sept. 30.

Nearly 70 scientist consultants participated in the workshops, including some members of the DNCP committee. Consultants were brought in from various specialty fields.

NCI SMOKING PROGRAM NEARS GOAL WITH "NEW GENERATION" BRANDS

Announcements recently by cigarette manufacturers of a "new generation" of low tar and nicotine brands indicate that the Smoking & Health Program supported by NCI may be approaching its primary goal, the development of "less hazardous," if not "safe," cigarettes.

The new brands are Merit, by Philip Morris, with 9 mg tar content; Kent Golden Lights, by P. Lorillard, with 5 mg tar; and Now, by Reynolds, with 2 mg tar.

The average tar content of U.S. brand cigarettes in 1974 was just over 18 mg, according to the Tobacco Institute. The average in 1955 was 45 mg.

Ernst Wynder, president of the American Health Foundation and a premier investigator in the field of smoking and health, has said that 15 mg tar content might be the level which would pose no threat to health provided the smoker consumed no more than a pack a day.

Gio Gori, who heads the Smoking & Health Program for NCI, disagrees and pegs the "safe" level at a maximum of 5 mg.

The new cigarettes seem to be more successful in retaining, or recapturing, the tobacco flavors of the higher tar brands. One informal, unofficial and probably unscientific survey conducted among NCI staff members turned up the opinion that Merit and Kent Golden Lights are acceptable to confirmed smokers, while Now probably is not. But a similar survey by ***The Cancer Letter*** found that Now was as good as the others and that all were acceptable. Two other brands, by the American Tobacco Co.—Carlton, with 5 mg, and Lucky Ten, with 10 mg—were equally acceptable.

Earlier attempts to produce cigarettes with tar content of 10 mg and less were not successful; smokers complained of the lack of taste. Gori's program has funded research on methods to keep the flavor while reducing levels of harmful components, including nicotine and carbon monoxide in addition to tar.

Manufacturers have conducted their own research in the engineering of new methods, but Gori said they have utilized techniques developed in the Smoking & Health Program to produce what he calls the "new generation" of cigarettes. These include the use of reconstituted robacco (in which the plant is ground up, bathed in a chemical solution which removes the harmful conponents and reformed into sheets); more advanced filters; better design of the

cigarette with less tobacco in each.

Gori said that manufacturers must continue to improve ways to put flavor back into low tar and nicotine cigarettes. Another problem is the development of a high porosity paper to permit burning at higher temperatures, which helps destroy harmful components before they are inhaled. The Smoking & Health Program is supporting research in those areas.

The so-called tars are the prime suspects in the carcinogenicity of cigarettes, along with nicotine. The deleterious effects on the cardiovascular system also has been attributed by some investigators to nicotine and to carbon monoxide. The average nicotine content now is about 1.5 to 2 mg; the Now brand has .2. Gori said that .5 mg probably should be the maximum. The average cigarette presently has about 18 mg of carbon monoxide; Merit has 11 mg and Now 7 mg, and Gori feels these should be reduced to 5.

Two years ago, Gori told ***The Cancer Letter*** that development of an acceptable less-hazardous cigarette, one that would not adversely affect the health of anyone who smokes no more than a pack a day, could be achieved within four years. He feels the Smoking & Health Program is still on that schedule, and that within two years could start phasing itself out.

"I would love to be out of the business in four-five years," Gori said. "In fact, our budget projections are counting on it. We planned from the start that the entire program would be completed in 10 to 12 years."

It is hard to overstate the significance of the program's achievement, if in fact truly less hazardous cigarettes are developed and successfully marketed. There are 84,000 lung cancer deaths in the U.S. every year; most of the victims were heavy smokers. Some investigators blame other tumors on cigarettes—mouth, laryngeal, bladder, among them. At least half of all fatal heart attacks involve smokers, as do most cases of emphysema. In all, cigarettes have been blamed for as many as 500,000 premature (before age 65) deaths a year in the U.S.

Eliminating cigarettes as a health problem would be one of the most stunning achievements in disease prevention of all time. And NCI is spending only $7 to $8 million a year on it, a figure Gori says is adequate.

Wynder feels the trend downward in cigarette-related deaths has already started. He told the Tobacco Working Group (which advises the Smoking & Health Program) last year that "today's cigarettes not only yield less tar and nicotine than those of 20 years ago, but because of changes in the manufacturing processes and the selection and blending of the tobacco used, they also yield fewer tumors in experimental animals. ∴ At least in part as the result in reduction of tar yield and tumorgenicity, lung cancer rates are going down in the 35-39 and 40-44 age groups among males. Similar findings should exist for other smoking related diseases."

A spokesman for the Tobacco Institute acknowledged that Gori's program has been effective in coordinating the technology that has led to the new cigarettes. He said the advent of these new brands proves the worth of permitting the industry to follow (not without considerable stimulation) the demands of the market place, rather than impose mandatory limits on tar and nicotine content, as the National Cancer Advisory Board has asked.

"Instead of outlawing cigarettes over a certain level, which would make them more desirable to many, we permit the market place to establish those levels," the industry spokesman said. "That's been going on for 20 years, and the average tar content has been reduced by more than half."

It didn't just happen, however. There was the Surgeon General's report, roundly condemning cigarettes as a health hazard, plus the antismoking efforts of the American Cancer Society, other health organizations, countless teachers and preachers, and the banning of TV and radio cigarette advertising. If all this didn't make people stop smoking, it at least made them aware that some cigarettes were safer than others.

The cigarette industry, to its credit, helped no small amount by putting most of its advertising money behind the safer brands. In 1974, when the industry spent $252.6 million on advertising, three-fourths of that money was spent on brands at or under the average of 18 mg tar content, according to Tobacco Institute figures.

In 1974, 85% of cigarettes sold were 20 mg or less in tar content; 60% were 18 or under, and 15% were under 15. Only 15% were over 20.

SENATE BILL WOULD PROHIBIT POLITICAL APPOINTMENTS TO ADVISORY COMMITTEES

When the Senate last month passed HR 7988, extending for two more years authorization for increased heart, lung and blood disease research, Maryland Republican Sen. Charles Mathias pushed through an amendment he said was needed to "prohibit HEW from appointing any individual to any NIH policy advisory committee on the basis of partisan or political affiliation."

Mathias quoted an article in *Science* which stated that for at least three years, politically appointed staff members in the HEW secretary's office have rejected nominations to NIH advisory committees. The article noted that there are about 36 vacancies on the advisory committees of the various NIH institutes. It quoted an Administration official as justifying political clearance of advisory committee members because they are "an adjunct to the Administration and there has to be some feeling that appointees will not be an embarrassment to the secretary or to the White House."

Mathias objected to that line of thinking. "The Congress did not establish the advisory committees at NIH for the purpose of supporting, defending or encouraging the interests of the President, the secretary of HEW or any other political figure," Mathias said in submitting his amendment. "These committees are expected to provide the best possible advice they can, based on their experience and knowledge.

"The public should expect that any appointment to an NIH advisory committee should be based upon the qualifications and ability of the candidate and the particular duties which the committee shall perform," Mathias continued. "At a time when public confidence in the government is at an all time low, and the need for high performance by government is at an all time high, the area of science and health should not be brought into pork barrel politics.

"I am aware that from time to time public officials, including members of Congress, will recommend individuals to serve on advisory committees. These recommendations, however, are offered with the understanding that the appointing authority will measure the candidate's qualifications against the requirements of the position and make his or her decision based on the merits."

The amendment states, "All appointments to advisory committees established to assist in implementing the Public Health Service Act, the Mental Retardation Facilities and Community Mental Health Centers Construction Act of 1963, and Public Law 93-282 shall be made without regard to political affiliation."

The National Cancer Act is part of the Public Health Service Act and thus NCI advisory committees, including the National Cancer Advisory Board, would be covered by the amendment if it becomes law. At present, there is only one vacancy on the NCAB, although six others will become vacant after the March meeting.

NCAB members are appointed by the President, not the HEW secretary. In the past, the President has depended on the recommendations of Benno Schmidt, chairman of the President's Cancer Panel. Schmidt submitted names for the one existing and six impending vacancies to the White House last October; no word has been transmitted to NCI yet as to whether or not they are acceptable.

Terms expiring are those of scientific members Harold Amos, Irving London, Gerald Murphy and Philippe Shubik, and lay members Elmer Bobst and Donald Johnson. The lay seat held by former New Hampshire Sen. Norris Cotton has been vacant since last summer, when he resigned to accept a temporary reappointment to the Senate during the controversy over that state's senatorial election.

The heart, lung and blood act contains at least two other provisions of considerable interest to those involved in the cancer program:

* Extension of the National Research Service Awards, which authorizes biomedical research training grants and fellowships.

* A section stripping the Food & Drug Administration of authority to regulate vitamins and minerals.

The measure had previously passed the House and will go to conference shortly after Congress reconvenes Jan. 19. The vitamin and mineral section is one of the major differences between the two bills.

Contract Awards

NCI RENEWS TWO BIG CONTRACTS WITH MICRO, ONE WITH MELOY

NCI announced three contract renewals in excess of a million dollars each last week, two of them to Microbiological Associates totaling $5.7 million.

Three-year renewals were awarded to Microbiological for viral-chemical carcinogenesis studies, $2.4 million, and studies on the isolation and characterization of type C viruses and diagnostic testing, $2.3 million. The figures are for the entire three years.

Meloy Laboratories received a one-year renewal of its contract for support services to maintain studies of spontaneous and virus induced neoplastic transformation for $1.2 million.

Other contract awards:

Title: Biosynthesis of oncorna proteins in mouse and human cells
Contractor: Univ. of Texas System Cancer Center, $277,426.

Title: Development of a method for large scale production of DNA polymerase I from E. coli
Contractor: Stanford Univ., $53,758.

Title: Furnish support services for studies of type-C, RNA tumor viruses
Contractor: Microbiological Associates, $329,682.

Title: Chemoimmunotherapy of acute myelocytic leukemia
Contractor: Mount Sinai School of Medicine, $293,971.

SOLE SOURCE NEGOTIATIONS

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

Title: Operation of Louisiana tumor registry
Contractor: Charity Hospital of Louisiana, New Orleans.

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